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ANATOMICAL AND EXPERIMENTAL OBSERVATIONS ON AIR EMBOLISM[1]

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AIR emboli, as a complication of thoracic operations, are probably more frequent than is generally recognized. In fact, Reyer and Kohl believe that many of those cases reported as pleural shock are, in reality, mild cases of cerebral embolism as the signs and symptoms in both conditions are very similar. In spite of this apparent frequency, it is unusual to have the opportunity of making a careful anatomical study of a clear cut, marked instance of air embolism followed by sudden death. For this reason, and because of associated intracranial vascular lesions, the following case is recorded. It led to an attempt to obtain a visual conception of living events in air embolism. Consequently, measured quantities of room air were injected into the aortic arch in a series of rabbits, while the vascular bed of the duodenal mesenteric loop was observed microscopically *in vivo*.

This was accomplished by using the ingenious apparatus devised by Ricker (10) and his co-workers, which permits the examination of tissues bathed in Ringer's fluid at a constant temperature, so that nearly physiological conditions prevail at the start. These experiments indicated that air emboli represent moderate or strong vascular irritants which produce a series of effects which are in all respects similar to those produced by other mechanical, chemical, or bacterial irritants, as described by Ricker (11), Koch and Nordmann (4), A. Dietrich (1), and others. The similarity of the exudative vascular lesions in the histological preparations of these experimental animals, to those of the intracranial vessels in the autopsied case, suggests that a similar neurovascular mechanism is concerned. These experiments are recorded therefore in conjunction with this case report because they seem to emphasize the importance of a neurovascular mechanism which is concerned in lesions associated with diffuse air embolism.

I. CLINICAL-ANATOMICAL SECTION

Summary of case record. The patient was a male aged 25 years. For 8 years following a right lobar pneumonia he had repeated attacks of bronchitis. About February, 1931, he developed a typical right sided pleurisy. During the next 6 months he had several recurrences and by October a lipiodol injection showed a diffuse bronchiectasis throughout the right lower lobe with pleural effusion. A right phrenicotomy was done in February, 1932, and a month later the lower lobe was partly resected. Following this partial lobectomy, he had a slow, gradual convalescence due to a bronchocutaneous fistula with empyema. By March, 1933, he had almost regained his normal weight, but lipiodol injections showed an extension of the hypertrophic bronchiectasis throughout middle lobe and remainder of the lower lobe. He continued to have abundant foul sputum. It was decided to do a right middle lobectomy. During the dissection of the lung from the very adherent pleura the main pulmonary vein was inadvertently cut. "There was a brisk sharp

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Fig. 1. Roentgenogram of skull taken 8 minutes after death. Note the pale fine linear network which is indicative of air in meningeal vessels, and in region of carotid arteries.

hæmorrhage accompanied by a whistling inspiratory sound. It took about 15 seconds before the Kocher clamp could be applied to this bleeder. Within a minute the anæsthetist reported that the pulse had fallen to 40, and blood pressure had risen to 160 systolic. Within 3 minutes of this hæmorrhage, the patient was declared dead."

X-ray pictures of the skull and chest were taken at once. The latter showed no evidence of air in the heart or any of the thoracic vessels. Stereoscopic pictures of the skull, however, showed shadows resembling air outlining the anterior portion of the circle of Willis and extending along the course of the middle cerebral arteries. The air in smaller meningeal vessels appeared as an irregular network of fine pale lines which were most definite over the parietal and temporal areas (Fig. 1).

Synopsis of autopsy findings, 5 hours postmortem. The body was of athletic habitus, and moderately well nourished. There was a recent curved gaping incision from the upper vertebral angle of the right scapula extending downward and forward to the anterior axillary line at the level of the seventh rib. Segments of the fifth and sixth ribs each about 8 centimeters long had been recently removed posteriorly, exposing the pleural cavity which was covered with firm grey tags resembling recently torn adhesions and fluid blood.

The lower half of the lower right lobe of the lung was firmly adherent to the medial half of the diaphragm, while the upper half of this lobe had been removed leaving a stump from which several open bronchi projected. Just below the large lower bronchus, was exposed the main pulmonary vein in which was a linear transverse slit, 5 millimeters long. A probe was readily passed through this clean cut opening into the left auricle of the heart.

Fig. 2. Photograph of diffuse bilateral subarachnoid hæmorrhage. The section removed from right parietal cortex shows gross hæmorrhage entirely confined to meninges.

The heart weighed only 270 grams. The right side contained a small amount of cruor clot and fluid blood, while the left was collapsed and contained a small amount of bright red, finely frothy, fluid blood and a few pale red, irregular, semi-solid masses of coagulum. The coronary arteries contained short and long columns of air separated by fluid blood, and there was slight bulging of smaller arterial segments in which the air was located.

The intracranial contents were examined before the thoracic or abdominal cavities had been opened so that the presence of air in these vessels could not be attributed to a replacement of lost blood from any proximally cut vessels. On removal of the calvarium and reflection of the dura mater, special care was taken not to cut the leptomeninges or brain substance. All emissary veins in the subdural space were ligated before being cut. Lying in the subarachnoid space over the frontal and parietal convolutions on both sides and extending out from the longitudinal fissure were diffuse areas of dark red fluid blood (Fig. 2). The arteries between the cortical convolutions in the leptomeninges of both frontal and parietal areas contained long and short dilated columns of air, between which was fluid blood. Similar air columns and fluid blood filled the arteries of the circle of Willis and extended mostly throughout the anterior and middle cerebral branches. No air could be seen in the very engorged meningeal veins or venous sinuses.

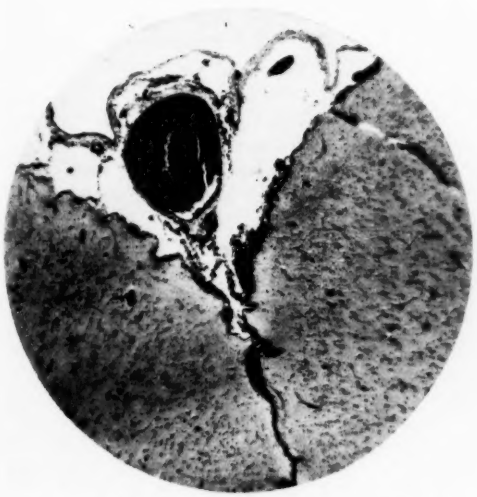

Fig. 3. Right frontal meninges and cortex. Note the ed cells which are lying free in the subarachnoid space nd which are surrounding the penetrating cortical ves- els. Also note a dilated meningeal vein filled with lood. ×35.

Fig. 4. Right frontal cerebral cortex. Serum fills and surrounds a vein in upper field and red cells surround a vein in lower field. Between these is a large oval space surrounded and partly filled by red cells. Fragments of a vessel wall are also in this space. ×40.

The brain was suspended in 10 per cent formalin for 5 days and then sectioned transversely in thicknesses of 1.5 to 2 centimeters. These sections showed a few small petechial perivascular bloody foci in the cortical gray matter of both frontal and parietal convolutions and the vessels were everywhere very engorged with blood.

Microscopic findings. In general, the histological examination of various organs confirmed the gross findings and will not be described in detail. The vascular changes in many histological sections from various parts of the brain and meninges were examined in the ordinary hæmatoxylin eosin preparations and also in large frozen sections of nearly half the cerebral hemisphere (Christeller method). These large sections were stained by the Van Gieson technique in order to avoid the shrinkage associated with dehydration. The following noteworthy vascular changes were recorded: (a) Large and small meningeal veins were markedly dilated and filled with well preserved red blood cells and very few leucocytes. (b) The red blood cells also lay in the subarachnoid space and in many places extended around engorged penetrating small vessels in the cerebral cortex (Fig. 3). (c) Many small cortical arteries and capillaries contained serum and red cells while others were collapsed. Well preserved red cells completely surrounded some compressed small veins, and where these perivascular red cells were most extensive the central vessel had partly disintegrated (Fig. 4). In none of the brain sections examined did the perivascular red cells surround arteries.

Anatomical summary. Intracranial and coronary arterial air embolism following incision into the right pulmonary vein during middle lobectomy. Subarachnoid bilateral hæmorrhage, both frontal and parietal. Petechial perivascular cerebral venous hæmorrhage with marked passive hyperæmia. Exudative productive pleurisy of the right side. Hypertrophic bronchiectasis of the right middle lobe and of the upper half of the lower lobe with an old partial lobectomy and persistent bronchocutaneous fistulæ.

II. EXPERIMENTAL SECTION

A. *Technique.* In order to obtain more definite knowledge of the vascular mechanism of air embolism, a technique was adopted which permitted a magnification up to 350 diameters of the rabbit's mesentery while air was being injected into the systemic arterial system. This modification of the Ricker apparatus by Loeffler and Nordmann was particularly applicable in these experiments for at least two reasons: (1) the microscopic vascular changes could be followed throughout the air injections *in vivo;* (2) with practice, the operator could perfect a technique that permitted him to start with a vascular mesenteric bed that was almost a physiological preparation.

Fig. 5. Arteriole in duodenal loop of rabbit's mesentery. Note the conglutinated mass of red cells behind the dilated segment containing the air embolus. ×135.

Air was injected into some part of the aortic arch through a long glass cannula which was inserted into an opening in the lower end of the right carotid artery just over the sternum. Particular care was taken to dissect off the vagus nerve and its depressor fibers from the carotid sheath without undue trauma. The best results were obtained when the cannula was inserted into the descending part of the aortic arch. Apparently because of the greater fixation of the clavicle and sternum in larger rabbits, this favorable position was obtainable only when the animal weighed not more than 1500 grams. To insure this position it was necessary to insert the cannula backward and to the left without undue manipulation.

In order to prevent air reaching the intracranial vessels and causing very rapid death, it was also necessary to ligate the left common carotid artery, having first dissected it away from the vagus nerve and its depressor fibers. When the cannula could be inserted into the descending aorta, however, it was found unnecessary to ligate the left carotid because it was closed mechanically by the position of the cannula.

A series of 12 rabbits were slowly injected, at irregular intervals, with measured quantities of room air, which entered some portion of the aortic arch while microscopic vascular changes in the duodenal mesenteric loop were carefully recorded. At death the duodenal loop and its attached mesentery were at once removed and fixed for 2 hours in Bouin's fluid. It was then transferred to 10 per cent neutral formalin for at least 6 hours. The larger vessels were then carefully cut away and the mesenteric fragments stained in aceto-carmin for 8 to 10 minutes. (The aceto-carmin is prepared by saturating a boiling 45 per cent solution of acetic acid with carmin and filtering when cool.) The tissue was then mounted moist in Farrant's or Apathy's fluid. In this way it was possible to study in further detail the histological sections of the same mesenteric areas that had already been examined *in vivo*. There were found to be two advantages to this fixation and staining technique: (1) It involved a minimum of shrinkage because the tissue was not dehydrated. (2) The picric acid accentuated cell outlines, while the aceto-carmin stained nuclear structures and red blood cells with a very fine definition.

B. *Observations.* Our observations may be conveniently grouped into (a) those which were common to all the series, and (b) those which applied only to a few or to individual experiments. Three important features must be described in further detail:

1. *Distribution and fate of air emboli.* In no instance did the room air reach further than the mesenteric arterioles. Capillaries and venules were persistently free of air. It tended to remain in long columns in the muscular arteries and was only slowly carried into the smaller arteries and arterioles. This slow movement was probably partly due to the peripheral arterial pressure as suggested by the closely conglutinated mass of red cells behind the column of air (Fig. 5). It was also partly due to surface tension resistance as suggested by the bulging of the vessel wall at the site of the air column (Figs. 5 and 10). As these air emboli were slowly carried toward the arterioles, they were broken with difficulty into smaller lengths usually at arterial branchings so that they often appeared to block or straddle branching arteries.

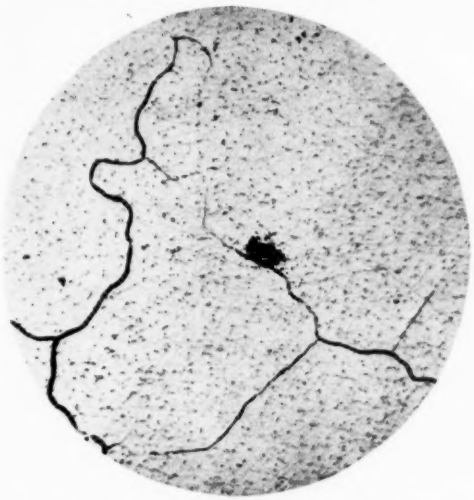

Fig. 6. Punctate hæmorrhage in capillary of rabbit's mesentery. Note the red cells extravasated from the most engorged part of a terminal district. ×55.

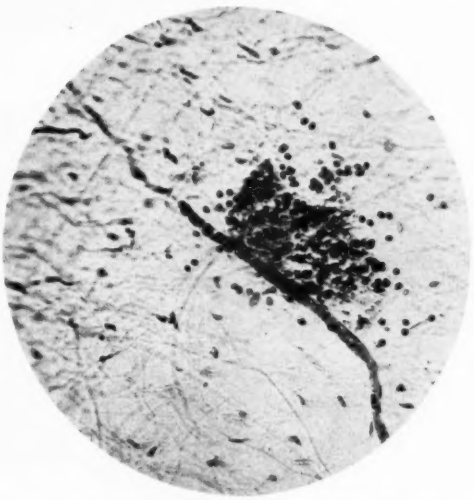

Fig. 7. Same punctate hæmorrhage shown in Figure 6. Note the intact vessel wall, engorged capillary, and collapse beyond the site of extravasated red blood cells. ×215.

Contrary to the observations of Hewson we could neither establish any definite coagulative action of the air on the blood nor was there any special relation of air emboli to the agglutination of red cells. In many microscopic fields transient stasis lasted as long as half an hour on either side of an air embolus with conglutination of blood cells, while in other fields this conglutination was followed by rapid and extensive agglutination. The very early separation of blood cells from fluid constituents in the arteries was notable, however, in every experiment. When agglutination occurred (following permanent stasis) the air was, of course, blocked in the arteries; but when conglutination occurred (during prestasis or transient stasis) the air often slowly disappeared on reaching the arteriole. This disappearance always occurred at a fixed point at the peripheral end of the air column, and could only be explained as a diffusion of the air into the Ringer's fluid. When the column had completely gone, there occurred an immediate rapid increase in blood movement through the arteriole and its peripheral terminal district.

2. *Changes in caliber of vessels and in blood movements.* Following the air injection muscular arteries at once showed many long or short constricted segments of variable degree, some were completely closed while others were only slightly narrowed. These constrictions disappeared in 2 to 3 minutes. They sometimes remained at their original site, but more often progressed in slow, irregular peristaltic waves toward the smaller arteries; never, however, reaching into the arterioles. It was a notable fact that these transient constrictions were much more marked, and in some instances only occurred at all after the first injection of air. The smaller caliber of the muscular arteries was associated with a marked decrease in the speed of blood through them. The vasoconstriction extended also into the terminal segments so that in many areas the capillary bed was completely closed, while in other areas, capillary loops opened only for short intervals to permit the relatively slow passage along their course of separated masses of blood cells and fluid. Dilatation of the muscular arteries at the end of 2 to 3 minutes was associated with a gradual increase in the speed of the blood stream. The constriction of terminal segments was apparently independent of that of the muscular arteries because it was irregularly distributed and of

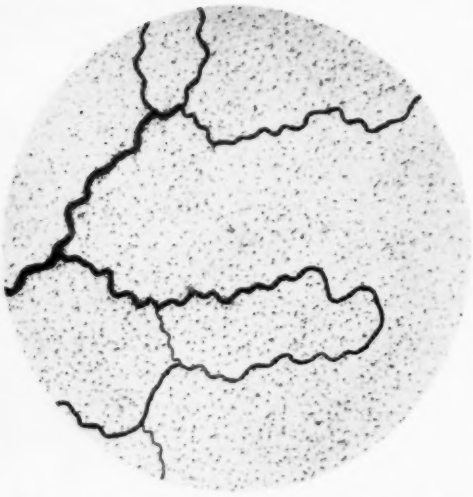

Fig. 8. The transmitted neurovascular effect of air emboli. Perivascular extravasation of red cells from venules of rabbit's mesentery in slightly punctate distribution. In this experiment air was confined to arteries too large to show in this photomicrograph. ×37.

somewhat longer duration. As these segments finally dilated, the blood flow became at first more rapid and the entire vascular bed was in a state of arterial hyperæmia. The presence of air in the dilated arteries, however, led to an abrupt slowing in movement of the blood stream. This often reached the degree of prestasis and stasis as the air was slowly carried into smaller arterial segments.

The effects of this mechanical obstruction of an air embolus during these changes in the caliber of vessels and in blood movements are well illustrated in Figure 9. In the living preparation this column of air could be followed as it progressed slowly along the arteriole to the center of the microscopic field shown in the photomicrograph. We assume that the complete obstruction caused by the embolus reduced the pressure in these terminal segments to zero because the forward movement of blood suddenly ceased through these anastomoses when the embolus appeared. The smaller veins, however, became intensely engorged by an apparent regurgitation of blood from larger venous segments. During the interval of prestasis, diapedesis of blood cells took place from the venules and adjacent small veins. This continued until permanent and complete stasis developed in the entire vascular district. There is no doubt that capillary as well as venous bleedings may sometimes occur just beyond the embolus. Such a picture is seen in Figure 10 where a capillary is surrounded by red cells as it branches from a dilated arteriole which is filled with air.

3. *Perivascular hæmorrhages.* The extravasation of a few white and many red cells from the capillaries and small veins occurred in every experiment, first, during the very slow blood movement associated with constriction of arteries and terminal segments, and second, during the later prestasis associated with the mechanical obstruction by air. These extravasations showed several notable features: (a) Their location. The blood cells escaped from capillaries, or the venous side of the terminal districts, or from their continuing larger veins, but never from the muscular arteries or arterioles. (b) Their microscopic appearance. The cells were arranged in more or less discrete focal punctate masses adjacent to the vessel. An extreme example of these focal petechial hæmorrhages is seen in Figures 6 and 7, while it is still apparent but less obvious in Figure 8. (c) Their origin and relation to air emboli. In no instance could actual defects be seen in the vessel wall at the points of blood cell extravasation, either *in vivo* or in the fixed preparations. The actual diapedesis of red cells through the vessel walls was often very difficult to follow, however, because of its rapidity and frequently because of its extensiveness. Thus the site of origin was often quickly obscured. Furthermore, the site of blood extravasation was always the site of the most intense vascular engorgement (Fig. 7) so that the vessel wall in the living preparation was always distended, thin, and poorly defined. It is of great importance, therefore, that in areas where the bleedings were not extensive enough to obscure the vessel walls, they appeared invariably intact (Fig. 8). It follows that the perivascular hæmorrhages are the result of diapedesis, thus simulating the white cell exudate described by Nordmann and Ruether in inflammations of the mesentery.

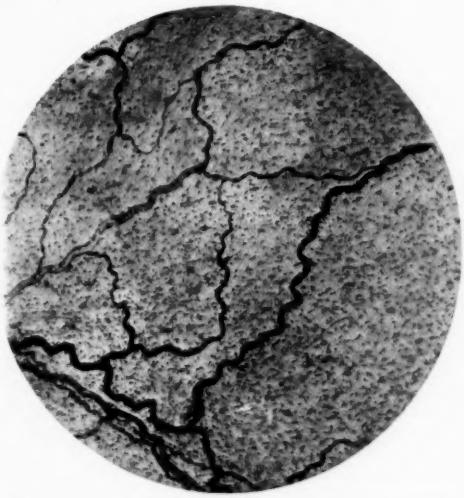

Fig. 9. The mechanical effect of air in a mesenteric arteriole. There is a long column of air in the arteriole on left half of the field extending to its capillary branching. Smaller and larger veins are intensely engorged and show perivascular zones of red blood cells. ×40.

Fig. 10. A dilated arteriole filled with air in its point of bifurcation, while a branching capillary is surrounded by scattered red cells. ×265.

It must be emphasized that the arterial vasoconstriction, diapedesis, subsequent dilatation, and hyperæmia outlined, were similar in all the experiments, and were independent of the mechanical effects of air emboli in the smaller muscular arteries. This independence was indicated by these vascular changes occurring in the complete absence of air in the *microscopic* fields of the mesentery in four instances. At autopsy, however, emboli could be readily seen partly filling those larger mesenteric arterial branches proximal to the vessels examined *in vivo*. (Compare Figs. 8 and 9.)

These experimental observations on air embolism may therefore be summarized as representing two distinct vascular effects. The first is traumatic and probably neurovascular, and the second is mechanical. (1) The traumatic neurovascular effect is independent of the nature of the irritant. It produces an immediate transient vasoconstriction of muscular arteries during which the slow peripheral blood movement (prestatic state) is associated with slight diapedesis. As fatigue of muscular arteries translates vasoconstriction to vasodilatation, there develops a progressive arterial hyperæmia. (2) The mechanical vascular effect is due to the specific agent, which is the air obstructing small arteries and arterioles. It also produces peripheral prestasis which is of rapid onset and sometimes prolonged. During this interval there occurs a more or less abundant diapedesis of red cells from the venous side of the terminal segments. This ends with the complete cessation of blood movement. Sometimes, however, a diffusion of air emboli through the arterioles leads to a return of the hyperæmic state.

DISCUSSION

The vascular changes in the clinical case of air embolism and the changes in the mesenteric vessels in this small series of experimental animals have several significant points of similarity. (1) The hæmorrhages in both instances were abundant surrounding engorged small veins and venous capillaries, but were never found about the muscular arteries. (2) Air was invariably confined to the intracranial arteries on gross examination of the autopsied case and it had a similar arterial distribution in the rabbits' mesenteries. Although one must accept with caution a com-

parison of tissue movements in animal experiments to human pathological processes, the similarity of these vascular changes under stimulus of the same irritant are strikingly suggestive of a similar mechanism concerned in the production of these vascular changes.

We have already pointed to the close resemblance which these vascular phenomena have to those observed under other conditions by Ricker. He has shown that any tissue irritant, whether bacterial, mechanical, or chemical, produces a definite series of vascular effects which may be taken as neurovascular reactions. Vascular irritants and responses are co-ordinated in duration and intensity. When an irritant of either moderate or strong intensity is applied to a tissue the blood vessel changes are identical to those described in these air emboli experiments. The slow blood movement in vasodilated terminal districts (capillaries and arterioles) is referred to by Ricker as peristasis, or peristatic hyperæmia. Leucodiapedesis, which occurs at this time, was limited in degree in our experiments because peristasis was followed quickly by a still slower blood movement, or prestasis. The remarkably rapid onset of the prolonged prestatic state following air emboli appeared definitely related to the constant and often extensive hæmorrhages by diapedesis. In this regard Ph. Schwartz and Neubuerger have pointed out the abundant and rapid hæmorrhages that may occur from intracranial vessels through apparently intact walls, a matter already fully appreciated by Cohnheim.

If the vascular irritant is removed before the constriction results in fatigue of the proximal muscular artery, as may be produced by a very small single injection of air, it will soon return to its normal caliber, the associated terminal vasoconstriction in arterioles and capillaries will disappear, and normal blood movement will be restored. If, however, the irritant is prolonged and intense, as was produced by relatively large re-injections of air in these experiments, the vascular changes resemble those described by Ricker in strong irritations, that is vasoconstriction in muscular arteries with vasodilatation (paresis) in the terminal segments (peristasis and prestasis). Thus we noted that muscular arteries were at first sometimes completely closed for short intervals. This represented an intense constrictor action which, on account of its rapidity of onset, could only be explained as the response to an irritant in proximal arterial branches. It was generally true that irritants of moderate intensity as produced by several small injections of air were prone to longer periods of prestasis and larger hæmorrhages than were irritants of strong intensity as produced by repeated larger injections.

It is not the purpose of this report to discuss at length the cause of death in air embolism, but it must be indicated that the numerous contradictions to be found in the literature on this point are mostly due to differences in resistance of test animals to air in their blood vessels. This may be partly accounted for by anatomical differences in their cardiovascular systems. Thus Naegeli points out that rabbits are much more sensitive to air emboli than are horses and dogs, and Wolf and others find that dogs will survive as much as 250 cubic centimeters of room air if injected slowly into a vein over 30 minutes, while rabbits will not survive 10 cubic centimeters of air injected over a similar period. In dogs the air is carried to the right heart and diffused in the peripheral lung capillaries and absorbed before reaching the systemic circulation, whereas in rabbits Kleinschmidt concludes that death is due to the mechanical impairment of function of the right heart, because much diffusion of air in lung capillaries does not occur. This is in general agreement with our observations following *arterial* air injections. All but two of our rabbits died with a mixture of regurgitated air and blood overfilling the left heart so that its muscular action was greatly impaired by the abnormal dilatation. The regurgitation was obviously favored by the position of the animal during the experiment.

In two animals air entered the intracranial arteries through open internal carotid branches and presumably caused death by sudden vascular stasis of districts peripheral to the emboli. This opinion is based on the justifiable assumption that the vascular changes in the intracranial arteries were in all respects simi-

lar to those observed in the mesentery at the same time. Death in these instances must therefore be attributed to the sudden loss of function of some vital center as the result of vasoparalysis with stasis. The analogous intracranial vascular changes which have been described in the autopsied case suggest a similar process, which would also account for his very sudden exit.

SUMMARY

1. A case of intracranial arterial air embolism has been described in which apparently air did not pass through the terminal segments but there occurred capillary and venous hæmorrhages by diapedesis.

2. The vascular changes seen *in vivo* in the duodenal mesentery of rabbits have been described following arterial air injections of room air. The similarity of this anatomical picture to the intracranial vascular lesions in the human case indicate a similar *modus operandi*.

3. Air emboli in rabbits produce two independent vascular effects. The first is probably a neurovascular mechanism, and the changes are similar following any kind of irritant. The second is mechanical, and is due to the obstruction of arteries and arterioles by the specific agent.

4. The immediate cause of death has been briefly discussed.

I wish to express grateful appreciation to Professor E. W. Archibald, surgeon-in-chief of the Royal Victoria Hospital, for the use of the case records including the X-ray photograph, and to Mr. H. S. Hayden of the Department of Neurosurgery for the photograph of the brain. All the photomicrographs were made by Mr. Brian Thomlinson of this Institute.

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ASPIRATION BIOPSY

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IN 1930, we reported (5) 65 cases of malignant tumors in which we had obtained material for histological diagnosis by aspiration of the tumors with an ordinary 18 gauge needle and record syringe. Since that time, the method has been generally employed by the clinical staff of Memorial Hospital wherever indicated, and on January 1, 1934, positive diagnoses had been made by this method in over 1,400 instances (Table I). Ferguson, Sharp, and Coley and Sharp have reported on the aspiration of certain clinical varieties of tumors. Stewart has recently reported his pathological interpretation of aspiration biopsies done at our hospital. Klinger and Burch have described a modification of the method by which the uterine cavity is aspirated with a blunt tipped copper tube attached to a syringe. Forster has applied the method in suspected brain tumors, aspirating through a small drill hole in the skull. Judging from the general acceptance of the method in all clinical departments of our institution, we feel that it has been proved to be a safe, reliable, and time-saving procedure in tumor diagnosis, and that it has been the only justifiable means of obtaining material for histological examination in the great majority of cases in which it has been employed.

The indications for aspiration biopsy are tumors which lie below the surface of normal tissue where tissue cannot be obtained otherwise, except by a surgical incision through normal tissue. In growths which are ulcerated on the surface, larger and more satisfactory biopsies can be obtained by the usual methods.

We believe that histological diagnosis is highly desirable in all, and absolutely essential in the majority of suspected neoplasms, in order that the proper therapeutic measures may be outlined. Biopsy by surgical incision through normal tissue may be followed by serious complications in the more malignant growths. Ewing has long been an active opponent of surgical biopsy made through normal tissues, especially in suspected tumors of the breast and long bones. His objections to surgical biopsy in such cases are that such a procedure modifies the clinical setting, breaks down the natural local barriers to the spread of the disease, and favors early metastases and fungation of the growth through the surgical wound. These views are quite generally accepted in regard to deeply situated tumors. We believe, however, that there is little risk in carefully removing a small biopsy from an exposed, ulcerated surface, or in entirely excising a movable, superficial, isolated node.

Aspiration biopsy has, we believe, few if any of the objections of surgical biopsy in tumors below the surface of normal tissue. The risk of dissemination of metastases through the tiny break in the capsule, such as will be caused by an 18 gauge needle, is comparatively slight. We have not observed any alteration in the clinical setting in any of the cases herein reported. The procedure is accepted casually by the patient as part of the routine examination. It can be done in a few minutes with little discomfort, if novocain is judiciously distributed along the more sensitive portions of the proposed needle puncture. No hospitalization is required and the procedure can be done in any clinic or office without any special preparation or apparatus, except an ordinary 18 gauge needle and record syringe.

One of its greatest advantages is in saving time in arriving at a definite diagnosis, so that the nature and order of the therapeutic measures may be immediately planned and discussed with the patient and family. The aspiration, itself, including the assembling of the apparatus and preparation of the patient, takes only about 15 minutes, and the smear can be stained and examined microscopically in about 10 minutes more. The numerous advantages of such an easy, rapid procedure, as compared to the laborious preparations and

delay following a surgical biopsy, requires no further comment.

TECHNIQUE

We have not found it necessary to alter our technique from that published in the original report. The special instruments required are an ordinary 18 gauge needle, 5 to 10 centimeters in length (which should be new or recently sharpened), and a 20 cubic centimeter record syringe. Needles of about 15 to 20 centimeters in length are sometimes required for aspiration at greater than average depths, as for instance in the lung or prostate. Glass slides are necessary for smearing the specimen, and a specimen bottle with 10 per cent formalin, if a portion of the tissue is to be treated as a regular biopsy.

The skin at the site of the intended puncture is painted with iodine, and a small area of skin infiltrated with 1 per cent novocain. In particularly sensitive regions, some of the local anæsthetic is injected continuously along the line of the intended puncture, down to the tumor. With a bistoury pointed scalpel (No. 11 Bard Parker blade), a stab wound is made through the skin with the instrument held at right angles to the skin surface. This puncture of the skin facilitates insertion of the needle and prevents contamination of the aspirated material by surface epithelium. An 18 gauge needle attached to a tightly fitting record syringe (with the piston closed) is then inserted and advanced slowly through the superficial tissues until the point is felt to enter the suspected neoplastic mass (Fig. 1). Guided by palpation with the disengaged hand, it is striking how readily a difference in consistence of the tissues can be felt, as the point of the needle enters a mass of neoplasm. When the point of the needle is felt to enter the tumor, the piston of the syringe is partly withdrawn so as to produce a vacuum (Fig. 2), and the needle is then advanced 1 to 3 centimeters further, depending on the anatomy and size of the tumor (Fig. 3). Maintaining the vacuum, the needle is then withdrawn to the same distance, advanced again, and withdrawn, thus maintaining the vacuum constantly and keeping the point of the needle within the tumor. Tissue from the tumor mass enters the needle and is held within it both by a punch action of the advancing needle and by suction of the vacuum. *Care must be taken that the vacuum is maintained while the needle is manipulated within the tumor. Aspiration by suction alone, with the needle at rest, is not sufficient to draw tissue into the needle, in most cases, and is the most common cause of failure to secure tissue.*

TABLE I.—POSITIVE DIAGNOSES OF CANCER MADE BY ASPIRATION BIOPSY AT MEMORIAL HOSPITAL

	Cases
Cervical nodes or tumors, including the parotid and submaxillary salivary glands	662
Breast	280
Bones	140
Prostate	55
Lung	41
Upper and lower jaws	27
Thyroid	17
Tonsil	15
Antrum	15
Base of tongue	11
Miscellaneous (axillary and inguinal nodes, intra-oral tumors, orbit, various soft part tumors, etc.)	142
Total	1405

Before the needle is completely withdrawn from the tissues, the piston must be slowly released, the syringe detached, and the needle withdrawn separately (Figs. 4 and 5), otherwise any remaining vacuum may cause the aspirated material to be suddenly drawn into and splashed over the interior of the syringe, making its collection more difficult. If the tumor is fairly firm in consistence, blood or tissue usually do not appear in the syringe, but the needle will be found to contain material. In soft and vascular tumors, a small quantity of blood mixed with fragments of tissue may enter the syringe while the needle is being advanced and withdrawn, or a solid cylindrical mass of tissue may appear.

After complete withdrawal of the apparatus, the syringe is partially filled with air, again attached, and the contents of the needle slowly and carefully expelled on to a glass slide (Fig. 6). If there is much resistance to expelling the plug of tissue from the needle by the air filled syringe, it is safer first to push part of the tissue out of the needle with the wire obturator, otherwise, with great pressure, the plug may suddenly pop out and be

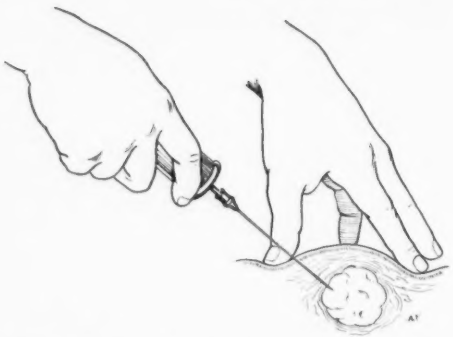

Fig. 1. An 18 gauge needle attached to a record syringe is inserted through the skin, guided by the palpating hand, until the point of the needle is felt to enter the tumor.

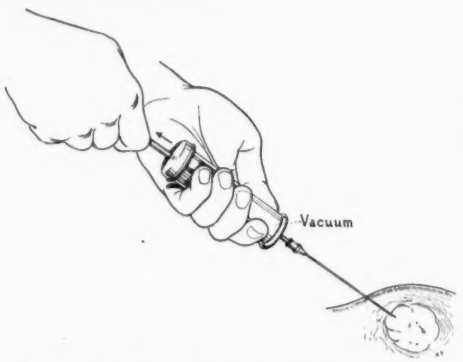

Fig. 2. With the needle stationary, a vacuum is produced in the syringe by partly withdrawing the piston.

lost. If only a smear of the specimen is desired, any excess of fluid or blood is carefully blotted off with gauze and a second slide placed over the first, and with *firm pressure*, crushed very thin and drawn once across lengthwise (Fig. 7). Tumor tissue having little intercellular supporting substance will usually smear out in a thin film which is quite characteristic. If the needle is found empty and there is any blood or other material in the syringe, a careful search should be made of this material, rolling the syringe between the eyes and a source of light. Any fragment of tissue may be then fished out on to the glass slide and smeared. If the material within the syringe seems to be composed of blood, this may be poured into a centrifuge tube and allowed to clot. The clot is later removed and sectioned like any large biopsy, and will be found to contain all tissue fragments firmly bound together.

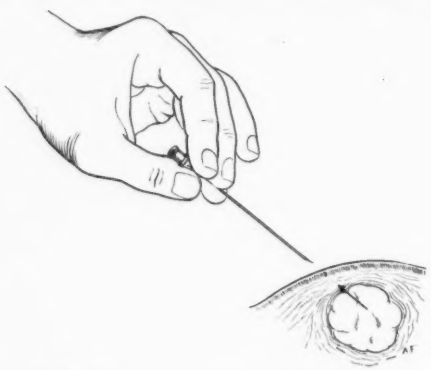

Fig. 5. The needle, which supposedly contains a plug of tissue from the tumor, is then withdrawn separately from the tissues.

Preparation of the specimen. The material may be prepared for examination by two methods: one, the immediate fixation and staining of the smeared slide, and the second, the collected fragments, either alone or embedded in a blood clot, are fixed and treated as any small biopsy. Patton routinely expresses the plug of tissue from the needle into a centrifuge tube containing 1 to 2 cubic centimeters of blood freshly drawn from a vein.

In our earlier observations, we attempted to secure fixed paraffin preparations for confirmation of the stained smear in all cases. After further experience of our pathological staff in interpreting the smears, we have omitted the more tedious and time consuming paraffin sections, except in certain cases in which such preparations would be of particular value or interest in diagnosis. Since one of the chief values of the method is the immediate reading, the stained smear will probably be found more generally practicable.

The immediate method. The fresh tissue fragment on the glass slide is smeared by firm flat pressure by another glass slide drawn once across (Fig. 7). The smeared slide is fixed by heating gently over a gas flame until warm and dry, and is then prepared according to the following technique:

1. Alcohol (95 per cent)—one minute.

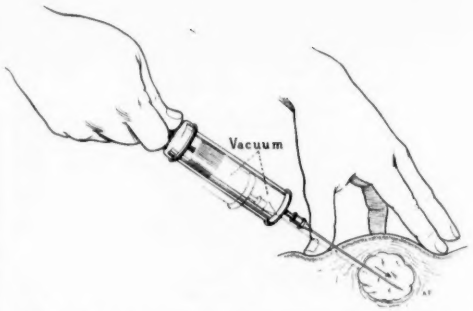

Fig. 3. Maintaining the vacuum, the needle is then advanced a distance of 1 to 3 centimeters depending upon the size of the tumor.

Fig. 4. Maintaining the vacuum, the needle is then withdrawn to the starting point. This manipulation may be repeated once or twice, with a slight change in the direction of the needle. The vacuum in the syringe is gradually released and the syringe is detached from the needle before withdrawal.

2. Water—one minute.
3. Hæmatoxylin—one minute.
4. Water—one minute.
5. Check by microscopic examination of the cellular stain, and if sufficient, proceed, or if insufficient, return to hæmatoxylin for deeper staining.
6. Eosin—one minute—check stain microscopically.
7. Alcohol (95 per cent)—one-half minute.
8. Carbol-xylol—one-half minute.
9. Xylol—one-half minute.
10. Mount with Canada balsam and cover glass.

The longer method. The remainder of the specimen, consisting of the collected tissue fragments or the blood clot containing them, is treated as any small biopsy, being carried through the stages of alcohol fixation and embedding in paraffin, great care being taken to collect and mass every minute particle of tissue, since a positive diagnosis may be obtained from the smallest fragment. Absolutely fresh 52 to 56 degrees C. paraffin should be used for embedding, and all particles massed together on the block and cooled immediately on ice. Every section cut from the block should be examined for fear that in dealing with such small particles, one might lose the opportunity of making a positive diagnosis. We usually cut 6 to 8 sections and place them on a single slide. These are carefully examined and further sections cut, if the first are negative, and more material remains on the block.

In case a reading is desired earlier than by our routine laboratory technique, we use the following method of preparation which requires about 3 hours.

The quick paraffin method:

1. Formalin 10 per cent—ten minutes.

Fig. 6. The needle is again attached to the syringe and the plug of tissue is expelled on to a glass slide.

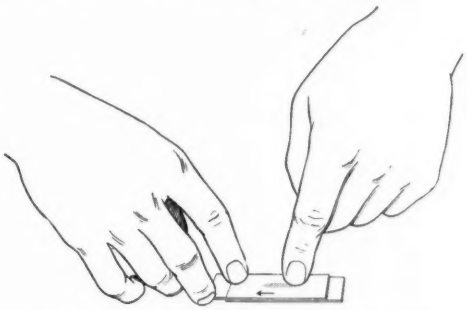

Fig. 7. A portion of the tissue fragment is smeared by firm, flat pressure with another slide, drawn once across, for immediate staining. A portion of the plug may be placed in alcohol for fixation and section by the usual method.

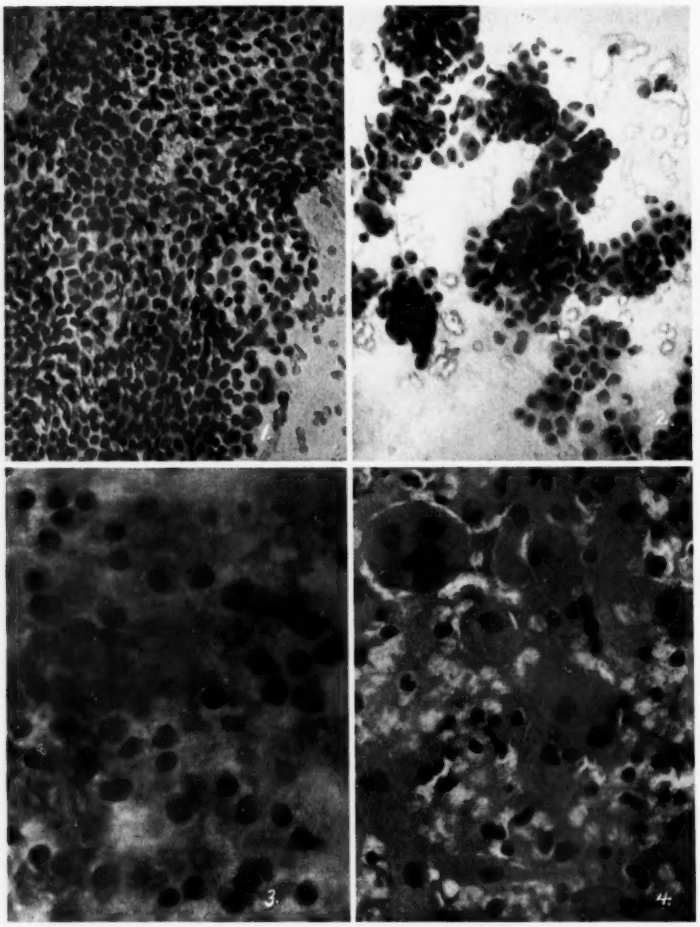

Fig. 8. Stained smears of aspirated material. *1*, Fibro-adenoma of breast; cells small, regular, coherent. *2*, Carcinoma of breast, cells hyperchromatic and loose. *3*, Plasma cell myeloma. *4*, Gaucher's splenomegaly.

2. Alcohol 95 per cent—two changes, ten minutes each.
3. Xylol—two changes, one-half hour each.
4. Paraffin 56 degrees C.—two changes, one-half hour each. (First three steps in incubator 37 degrees C.)
5. Cut and stain.

PATHOLOGICAL INTERPRETATION

The interpretation of smears of material obtained by aspiration requires, first of all, a sympathetic attitude of the pathologist, and refusal on his part, to consider the procedure, naturally means that no progress can be made in this rather difficult field of diagnosis. Stewart has discussed, in detail, the pathological interpretation of aspiration biopsies. The pathologist may readily obtain experience in this field, by smearing fresh fragments of tumors from the operative or autopsy specimens in his laboratory.

One might ask what information may be obtained from a smear of aspirated material. One hopes at least to determine whether or

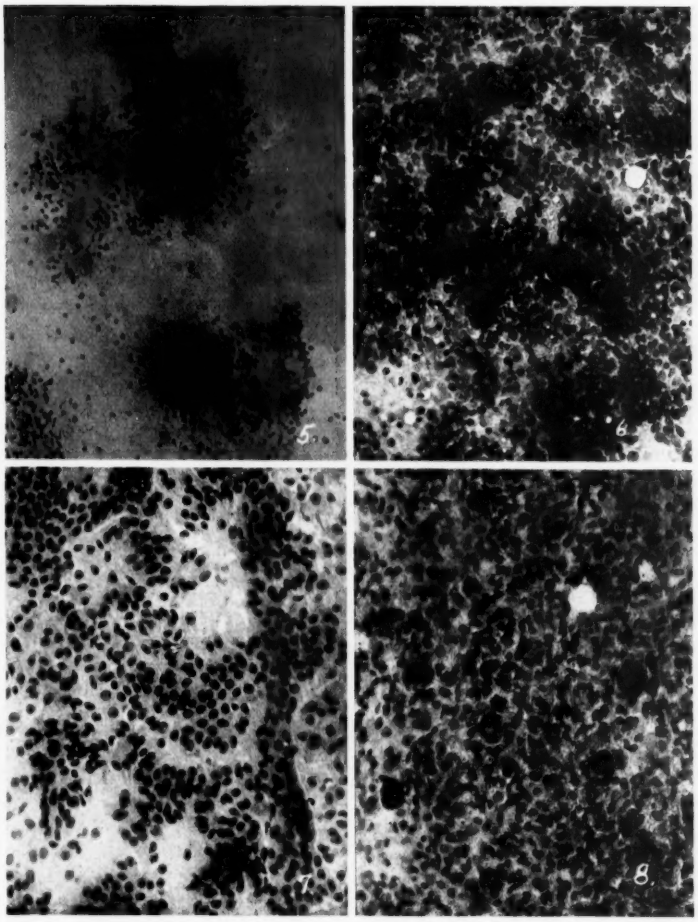

Fig. 9. Stained smears of aspirated material. *5*, Mixed tumor of parotid; much mucin and atypical cell group (low power ×110). *6*, Transitional cell carcinoma, tonsil. *7*, Epidermoid carcinoma, lung. *8*, Pigmented melanoma, large pigmented cells.

not a malignant tumor is present, and whether it is of epithelial or of connective tissue origin. In some instances, that is all one learns from the smear alone. If a plug of aspirated tissue is fixed, cut, and stained by the usual methods, the preparation differs from ordinary sections only in that it is small.

In our laboratory, no diagnoses are rendered from aspirated material without reasonably full clinical data, since an accurate knowledge of the exact source of the material is of major importance. Knowing the source, knowing what tumors are apt to occur in the region, and being fully cognizant of the histological criteria for diagnosis of such tumors from ordinary sections, one may form, from the various minutiæ of the smear, a sort of composite picture which permits a visualization of the probable histology of the process, and hence a diagnosis of the type of tumor. Difficult at first, this becomes easier with experience. Except that the cell arrangements

are lost, the diagnostic criteria are the same as in sections prepared in the usual manner.

If the aspirated material is partly liquefied or necrotic, histological diagnosis may be more difficult than with viable tissue, and requires interpretation derived from a consideration of the region involved, the treatment administered, if any, and a knowledge of the changes likely to have occurred under the circumstances. The following illustrations may be offered as to the possible interpretations: If a smear from an aspirated cervical node contains caseous necrotic material, rare large acidophilic flattened cells and numerous giant cells, the flat acidophilic cells suggest sloughing squamous carcinoma; the caseation and giant cells suggest tubercle. The combination indicates a broken-down, cystic cervical node metastasis of epidermoid carcinoma, probably irradiated, with necrosis and a foreign body giant cell reaction to necrotic squamous pearls. In another case, if the smear from an aspirated cervical node or mass in the region of the carotid bulb presents sloughing squamous epithelium and large sheets of lymphoid tissue, the diagnosis lies between metastatic carcinoma and branchiogenic cyst. Either will yield sloughing squamous epithelium.

Let us assume that no primary tumor can be found in the oral cavity or upper respiratory tract. When a metastatic node is sufficiently large to yield *sloughing* squamous cells, that is, when cystic degeneration has occurred, it will be found that the lymphoid elements of the node are completely replaced by the tumor. Hence, if we find *large numbers* of lymphocytes in the smear, the indicated diagnosis is branchiogenic cyst, since much lymphoid tissue is often present in the walls of such cysts. With this much information at hand, surgical exploration becomes justified.

The finer histological classifications and grading of tumors cannot be made from aspirations. For instance, one cannot hope to classify the various anatomical sub-varieties of mammary cancer. As a rule, the probable behavior of a lesion to radiation cannot be predicted, although at times this has been possible. It is possible to carry the discussion of diagnostic criteria through much of the realm of regional diagnosis of tumors by aspiration, but this would lead us into much descriptive pathological detail, which is foreign to the purpose of this paper, and which has already been published by Stewart.

CLINICAL APPLICATION

As previously stated, the procedure is indicated in any case of suspected malignant tumor in which the lesion lies below the surface of normal tissue. Its particular advantages in various anatomical localities merits a more detailed discussion.

Cervical adenopathies or tumors. In our clinic at Memorial Hospital, we receive a large number of cases referred because of enlarged neck nodes or cervical tumors. In most of these cases, a thorough search of the upper alimentary and respiratory tracts immediately discloses the primary lesion. In others, no primary lesion is found at this first examination, and the question of differential diagnosis rests among the following possibilities, as shown by our experience.

1. Metastasis from an undiscovered primary lesion of the upper alimentary and respiratory tracts.
2. Metastasis from a visceral primary, such as stomach, kidney, lung, etc.
3. Inflammatory hyperplasia of lymph nodes.
4. Malignant lymphoma—Hodgkin's disease, lymphosarcoma.
5. Adenopathy of the leukæmias.
6. Tuberculosis.
7. Syphilis.
8. Actinomycosis.
9. Primary cervical tumor—branchiogenic carcinoma, carcinoma of the thyroid, neurogenic sarcoma, liposarcoma, carcinoma of the submaxillary salivary gland, etc.
10. Branchiogenic cyst.

One should consider the laborious, expensive, and time-consuming procedures such as the Wassermann test, roentgenograms of the chest and gastro-intestinal tract, and blood counts necessary to rule out many of these possibilities, only to be forced eventually to depend on surgical biopsy. Immediate diagnosis is extremely urgent in the case of a lethal disease such as cancer.

We make it a routine procedure to aspirate all cervical adenopathies of unknown nature. The patient waits until the smear is stained and examined microscopically. If a report of "epidermoid carcinoma" is returned, the probabilities are that an undiscovered primary lesion exists somewhere in the upper alimentary or respiratory tracts, and repeated further examinations of the pharynx are made. Although cervical metastases may be quite evident, the primary lesion in the nasopharynx or at the base of the tongue may be so small as to escape detection by the first clinical examinations. Although treatment may be instituted to the cervical nodes, pending further examinations, the diagnosis is considered incomplete until the primary is discovered by repeated examinations.

Most cervical adenopathies in the adult are malignant and are usually metastatic from intra-oral or pharyngeal cancer. We have been able to make histologically verified diagnoses in clinically doubtful cases of such primary cervical neoplasms as branchiogenic carcinoma, carcinoma of the submaxillary salivary gland, neurogenic sarcoma, carcinoma of the thyroid, and liposarcoma. Strongly presumptive diagnoses may be made in the cases of Hodgkin's disease and lymphosarcoma.

In benign cervical adenopathies and tumors, aspiration is often of great assistance. Clear straw colored, or even slightly bloody fluid, from an apparently solid or cystic mass at, or slightly above, the carotid bulb, makes a diagnosis of branchiogenic cyst almost certain. The same type of material from a mass in the midline of the neck near the level of the hyoid bone indicates a thyroglossal cyst. Stewart of our pathological laboratories has repeatedly diagnosed tuberculosis, and on one occasion, actinomycosis, from the appearance of the smear. With such a lead, in the majority of these cases, we have been able to confirm the diagnosis by further clinical or laboratory examinations.

In clinics where neck dissections are practiced routinely, histological material is always available for record. In our clinic, neck dissections have been largely given up in favor of more conservative means. The metastatic nodes of the more anaplastic and radiosensitive varieties (especially pharyngeal growths) are subjected to external irradiation at the same time as the primary lesion. If they do not regress with the primary, radon gold seeds are then implanted, either after surgical exposure of the nodes, or through skin punctures. In either case, no surgical biopsy is done, and histological verification of the actual presence of cancer in the nodes is essential for record, if such treatment methods are to be evaluated accurately 3 to 5 years later. We therefore make it a practice to aspirate all such nodes for record. If the node is surgically exposed for the gold seed implantation, it is aspirated in the operating room, after its outer surface has been exposed, preparatory to implanting the seeds.

Tumors of the oral cavity, oral and nasal pharynges, and paranasal sinuses. Most tumors of the oral cavity are ulcerated on the surface from which a regular biopsy can be taken. On the other hand, we have repeatedly found carcinoma of the base of the tongue presenting as massive, palpable tumors with no apparent surface ulceration. In these cases, aspiration is readily accomplished through the midline of the neck just above the hyoid bone, thus avoiding a painful, difficult surgical incision into the tumor.

Carcinoma of the antrum may destroy its bony walls and produce marked swelling of the cheek without any surface ulceration. Quite commonly, such growths will be found ulcerated and fungating into the nasal cavity of the same side, from which a regular biopsy can be obtained. If there is no surface ulceration and the nasal cavity is clear, tissue can be obtained by aspirating directly through the cheek or hard palate at a site where bulging occurs, indicating perforation of the bony walls.

Carcinoma of the ethmoids commonly erodes the mesial wall of the orbital cavity and presents at, or just below the canthus, as a soft or cystic swelling under the skin, which may be aspirated for diagnosis.

Tumors of the pharyngeal wall, tonsillar region, palate, or cheek may present smooth, bulging surfaces without ulceration through which an aspirating needle may be easily and painlessly inserted (Fig. 9. *6*).

Adamantinoma, dentigerous cysts, and central giant cell tumors of the jaws are not always readily differentiated roentgenographically. Aspiration usually obtains sufficient evidence to permit a diagnosis when supported by clinical and X-ray findings. In suspected tumors of any of these regions, a diagnosis of a benign cyst or abscess is often made by aspiration.

Tumors of the parotid. Benign mixed tumors and true malignant carcinomata of the parotid are quite readily differentiated clinically, if the characteristic features of either one are present. However, we have repeatedly seen slightly nodular, firm, movable tumors of long duration which proved to be true malignant carcinomata of the parotid, capable of metastases. We have also observed cases of fairly soft, fixed tumors of short duration which were benign mixed tumors. A knowledge of the histological nature of a parotid tumor is of paramount importance in outlining treatment. Mixed tumors, if operable, are best treated by surgical excision, while true carcinomata are in most cases infiltrative in character, and total removal is impossible, except by radical and deforming operations which are commonly followed by prompt recurrence and widespread metastases. In our opinion, the latter should all be treated by irradiation. Aspiration biopsy renders a correct diagnosis in most cases, and permits of a rational plan of procedure (Fig. 9, 5).

Breast tumors. The procedure has assumed a definite part of the routine in the diagnosis of breast cancer at our hospital under the direction of the late Dr. Burton J. Lee. If the disease is well established so that the clinical diagnosis is assured and the proposed method of therapy is to be radical excision, aspiration biopsy is of no particular value from the practical standpoint, since the whole breast and axillary contents will be available for pathological examination after operation. There is, however, no contra-indication to its use in such cases in Lee's opinion.

Its chief value in breast tumors is in the diagnosis of doubtful cases. In this regard, one may consider the combination of clinical and psychological situations which are so frequently met with in breast tumors. A highly nervous and apprehensive woman who may have digested the current propaganda in regard to the early recognition of cancer, discovers a lump in her breast. She immediately consults her surgeon, or is referred to a surgeon, for an opinion. A definite mass is found in the breast which in all probability is cancer, but which in the surgeon's opinion, might be of a benign character. The surgeon is then faced with the following alternatives: To recommend a radical amputation of the breast for what might turn out to be a benign condition; to admit the uncertainty of his diagnosis and request a consultation; to secure permission for a local removal and frozen section, and an immediate radical amputation if the tumor is found to be malignant. In any case, an apprehensive patient and the family are kept under suspense until the operation is completed, and the surgeon proceeds under the mental handicap of uncertainty, which he must in all fairness, confess to the family at least.

If under the same circumstances, the surgeon suggests aspiration biopsy on the first visit, the atmosphere of doubt, uncertainty, and indecision will, in most cases, be removed. Permission for aspiration is readily obtained, if it be explained that it is a necessary "test," after which a definite opinion can be given. If the report of the smear is carcinoma, a confident attitude may be taken by the surgeon in regard to the proposed method of treatment. In other cases, an immediate opinion may be given that the condition is benign and local excision or observation only advised.

An operation, begun with a view to a possible radical amputation, and after frozen section, completed as a local removal of a benign tumor, will commonly result in an unsightly scar or deformity of the breast. Incision into the tumor for frozen section followed by radical amputation prolongs the time of operation, and from the theoretical standpoint, at least favors immediate and unnecessary risk of general dissemination.

In other cases of undoubted carcinoma, radical amputation of the breast may be contra-indicated because of some concurrent disease, the advanced age and poor general condition,

the evidence of pulmonary or bony metastases, or the youth of the patient. In these situations, the prognosis following surgery is uniformly bad, and at our hospital, their treatment by some form of irradiation is recommended. In Lee's and Adair's opinion, even surgical biopsy is to be avoided in these cases, since it modifies the clinical setting and renders subsequent irradiation by any method more difficult and unsatisfactory. Aspiration serves to verify histologically the clinical diagnosis of cancer in these cases for record (Fig. 8, *1* and *2*).

At the present time, immediate aspiration is employed almost as a routine diagnostic procedure on the breast service at Memorial Hospital, if the least possibility of mammary carcinoma is considered. Positive diagnoses of breast carcinoma have been obtained in 280 instances at Memorial Hospital. The procedure is employed not only for primary breast lesions, but for diagnosis of questionable axillary or supraclavicular nodes.

Lung tumors. Bronchoscopy has definite narrow limitations in the diagnosis of thoracic tumors. Positive diagnoses of lung cancer can be made bronchoscopically only if the growth arises in, or has ulcerated through, the wall of one of the lower or middle lobe bronchi, the trachea, or at the proximal end of either upper lobe bronchus, so that a biopsy can be removed. Except where the lesion presents itself so that a biopsy can be removed, bronchoscopic evidence is presumptive only. It must be admitted that monocular inspection through an instrument of such a narrow caliber as a bronchoscope would be considered entirely insufficient for diagnosis in the exposed accessible portions of the body, where adequate inspection and palpation are possible. If the tumor lies within the parenchyma of the lung or arises in an upper lobe bronchus, aspiration offers the only justifiable means of biopsy (Fig. 9, *7*).

For lung aspirations, longer 18 gauge needles of 15 to 20 centimeters are advisable. It would seem, on first thought, that there might be considerable danger in puncturing a large bronchus or blood vessel, but we have observed no untoward results in 41 instances. We have undoubtedly punctured the larger bronchi on several occasions, as evidenced by withdrawal of air into the syringe, and the spitting up of a few drops of blood. No serious or even significant effects were noted except as above mentioned. While we have always attempted to avoid the neighborhood of the vena cava or aorta, we have undoubtedly punctured blood vessels of considerable size in several instances, since the syringe partly filled with blood. In these cases, there was also a complete absence of any significant sequelæ.

Before an aspiration of a lung tumor is attempted, a careful study of the chest X-ray should be made, locating the tumor in its relation to the intercostal spaces and its position in the transverse axis. A stereo X-ray examination aids in determining its position in anteroposterior diameter so that it may be approached from the nearest point, either on the anterior or posterior chest wall. After a preliminary hypodermic of morphine and rather deep novocain infiltration of the chest wall down to and including the pleura, the procedure is usually best accomplished in a sitting position.

Abdominal tumors. The aspiration of abdominal tumors which might be superimposed by intestines would, of course, be a dangerous procedure, and we have not attempted it. In situations where the tumor certainly lies against the abdominal wall, without any possibility of intervening gut, there is no logical objection to the procedure. In 5 instances, we have aspirated masses in the liver which lay immediately next to the abdominal wall. Material, sufficient to prove the presence of carcinoma, was obtained in all instances, but the type could not be determined. We have twice aspirated the spleen for suspected Gaucher's disease (Fig. 8, *4*). Positive diagnoses were possible in both from the smeared material; these diagnoses were confirmed after splenectomy by one of us (Mason) in both cases. No general rule can be made for the advisability of aspiration in abdominal tumors, and the indications must be determined independently in each case. At laparotomy, tumors may be exposed from which, for some reason, the surgeon hesitates to remove a biopsy by the usual methods. Such tumors

may be aspirated for confirmation of the clinical diagnosis. Histological material showing cancer has been obtained on two occasions by the aspiration of tumors of the stomach wall, and in one instance, a mass in the wall of the sigmoid has been aspirated with a histological report of cancer.

Bone tumors. The classification of bone tumors by X-ray examination is sometimes impossible, and we know of no situation in which the differentiation between a benign and malignant tumor is more commonly attended by so much discussion and difference of opinion. We see no valid reason why such cases should not be subjected to immediate aspiration which, in many cases, will render superfluous any further discussion from the diagnostic standpoint. Without a definite diagnosis, opinion may be divided between amputation, local excision with curettage, and external irradiation only. Surgical biopsy of bone tumors is undesirable or a dangerous procedure, if the tumor should be malignant. Amputation of a limb for a suspected malignant tumor which proves to be benign, is a tragic error which may be avoided in many cases of aspiration. The local changes following the necessarily heavy irradiation for malignant tumors treated by that method alone, are certainly justified in certain instances, if a reasonably functioning limb may be spared thereby. The same sequelæ are, however, not always justified, if a benign tumor is treated in the same manner under a mistaken diagnosis.

Accurate classification as to type is not possible from the smear in bone tumors, except in some cases of benign giant cell tumors and endothelial myeloma, where definite cell forms or arrangements may be evident in the smeared preparation. However, if material is obtained, it is usually possible to differentiate between a benign and malignant growth. On such data, coupled with the history, physical examination and the roentgenographic findings, a correct diagnosis is obtained, sufficient, at least, to advise proper therapy (Fig. 8, *3*). Diagnoses in 140 instances of bone tumors have been obtained by aspiration in our hospital. In one case, a diagnosis of echinococcus cyst was made by aspiration of a tumor of the pelvic bones which had been repeatedly diagnosed by X-ray examination, in several clinics (ours included), as osteogenic sarcoma over a period of one year.

Coley and Sharp reported 35 cases of aspiration biopsy in bone tumors. They found it of advantage to use a short gas anæsthetic in certain cases in which some resistance was anticipated in puncturing the cortex of bone, which was only partially destroyed by the growth. A short gas anæsthesia is undoubtedly advantageous in the aspiration of many bone tumors, especially in apprehensive patients.

Carcinoma of the prostate. Biopsies from cancer of the prostate were formerly practically never obtained except after surgical excision of the gland or at autopsy. Cases in which patients were treated by conservative measures therefore lacked conclusive diagnostic data, in most instances. Ferguson has developed a technique for aspiration of the prostate through the perineum, and there are at this time, 55 cases in the records of our pathological laboratory. Ferguson uses a specially made 18 gauge needle, 15 centimeters in length, which may be locked on to the syringe, and containing an obturator. The skin and superficial tissues of the perineum are infiltrated with novocain, and the needle with the obturator in place, is inserted through the perineum with a guiding finger in the rectum, which palpates the enlarged prostate and directs the needle into it. The obturator is then removed and the syringe attached. The remainder of the technique is as we have described. No untoward after effects have been noted, even though Ferguson admits having inadvertently punctured the bladder on several occasions.

Miscellaneous tumors. Suspected metastatic nodules or tumors, recurrent after either surgical excision or irradiation, supply a fruitful field for aspiration (Fig. 9, *8*). In many of these cases, it is extremely difficult to differentiate between recurrences of malignant disease and masses of scar tissue, inflammatory lymphadenopathies, slowly absorbing hæmatomata, or traumatic fat necrosis. In such cases, one does not feel justified in subjecting the patient to surgical biopsy or in proposing surgical excision or further irradiation, without more conclusive evidence. Rather than

wait for more definite clinical evidence and a worse prognosis, the question can usually be definitely settled by aspiration.

Tumors of the skin are usually ulcerated and superficial, but we have repeatedly obtained tissue from deeply infiltrating basal cell carcinomata of the eyelids or the region of the canthi, where surgical biopsy would have been objectionable, because of laceration of the tissues. After aspiration, the patients were treated by implantation of radon seeds.

Histological examination of tissue is essential in the treatment of neoplastic disease, not only in outlining treatment, but for purposes of record. Only 5 year cases are considered as conclusive evidence of the value of any particular treatment method. Unsupported by biopsies, clinical diagnoses, 5 years old, whether made by oneself or by others, cannot avoid being viewed with some doubt, if the cases have done particularly well. At our hospital, statistics are based only on cases having histological examinations. Biopsy by surgical exposure is too often extremely ill advised when casually performed by a surgeon who contemplates giving no further treatment himself, and it should be severely condemned when done in this manner without careful consideration and definite purpose. Biopsy by needle puncture and aspiration has, we believe, few, if any disadvantages to the patient from the surgical standpoint, and has, in our experience, proved to be a safe, reliable diagnostic method in many cases in which surgical biopsy is contra-indicated.

SUMMARY

The indications for, and the technique of, biopsy by needle puncture and aspiration are described in detail. Over 1,400 positive histological diagnoses of cancer have been made by this method at Memorial Hospital.

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THE SYMPTOM-COMPLEX OF COMPLETE EXTERNAL PANCREATIC FISTULA

Report of a Case[1]

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THE physiology of the external secretion of the pancreas is now rather well known, but the clinical syndrome and the pathological significance of the loss of this important secretion to the body are still generally unrecognized if one can judge by the literature on the subject. It is our purpose to report a clinical example of this condition, substantiating in the human subject the recent experimental work done. The deductions to be drawn may go far to explain the clinical findings in many of the pancreato-biliary group of diseases.

EXPERIMENTAL INVESTIGATIONS

Pavlov and others early noted various digestive disturbances following the establishment of an open pancreatic fistula in dogs, but hypersecretion followed by death was regarded as an exceptional occurrence. Pratt showed in 1916 that the exclusion of the pancreatic juice from the intestine by section or evulsion of its ducts caused a marked disturbance in the absorption of nitrogen and fat. But it was not until 1926 that Elman and McCaughan (8) first clearly demonstrated that these adverse effects were due to the removal of some necessary substance from the body and its excretion in the pancreatic juice. When the entire output of the external secretion was excluded from the intestine by an improved fistula to the outside, death invariably resulted in from 5 to 8 days with marked metabolic disturbances. Using a more indirect method (acute duodenal fistula), Walters and Bollman likewise came to the conclusion that the loss of pancreatic secretion for any length of time was incompatible with life, whereas the loss of bile and duodenal secretion was without lethal effect. More recently, Gamble, Laqua, and Dragstedt (6) with their associates have carried on experimental work which has confirmed these results.

A uniform, lethal syndrome was exhibited after operation, characterized by striking anorexia, vomiting, marked asthenia and loss of weight, and pronounced dehydration. The significant metabolic changes were a rapidly progressive anhydræmia (plasma volume as low as one-fifth of total blood volume), a slight acidosis, a moderate decrease in the blood chlorides, and an elevation of the blood urea nitrogen shortly before death. Postmortem examination was invariably negative, except for mild chronic inflammatory and degenerative changes in the pancreas. In animals in which few or no deleterious effects were observed and death failed to occur following apparent complete external fistula, accessory ducts were found on sacrificing the animals, showing that the pancreatic loss was subtotal.

The pancreatic juice collected from these fistulas possessed practically no power to digest proteins, an observation which was first recorded in Pavlov's laboratory by Schepowalnikow and has since been repeatedly confirmed. It was shown that the inactive trypsinogen must be activated by enterokinase, a secretion of the duodenal mucosa, such being the normal mechanism. It has since been observed that trypsinogen may, in certain instances, be activated by bile, calcium in the blood or plasma, and by bacteria.

The essential cause of early death in these animals was not apparent. The comparatively slight alteration in the blood chemistry gave little evidence of the profound general disturbance noted. Analogies to high intestinal obstruction and to gastric or duodenal fistula were drawn, although in these conditions the blood chemistry changes were admittedly much more striking. However, Jenkins, working on high intestinal obstruction in dogs, prolonged life considerably by short-circuiting the pancreatic, biliary, and duodenal secretions below the point of obstruction, either

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permitting essential reabsorption in the lower bowel or preventing the formation of a toxin in the obstructed loop. Anhydræmia alone is known to alter the conposition of the blood and to lead to a fatal termination (15, 18, 27). Certainly this was one of the most marked disturbances in the dogs with lethal pancreatic fistula. It was generally agreed by most of the experimenters that the loss of salts, water, and protein by way of the fistula and gastric vomitus, and their failure of reabsorption in the lower intestine played quite an important rôle in the pathogenesis and early death in this condition.

This supposition was attested by the uniformly beneficial results which were obtained by the use of daily intravenous injection of Ringer's solution or of physiological salt solution. Under such therapy, the normal chemistry of the blood was maintained and life greatly prolonged. Apparent restoration to a normal state in a moribund dog was also secured by the *oral* administration of whole pancreatic juice, the intravenous infusion of which failed to have such a benefit.

CLINICAL STUDIES

External fistula of the pancreas was apparently unknown until the advent of abdominal surgery, with special reference to operations for inflammations, cysts, stones, and injuries of the pancreas. The necessary institution of drainage in such cases to prevent the discharge of pancreatic secretion into the abdominal cavity provided the source for such fistulas. The first mention of a human pancreatic fistula was by Rommelaere, a Belgian, in 1877. Pfaff reported the first case in this country in 1897. Interestingly enough, the fistula, which lasted only 48 hours, followed an operation by H. W. Cushing for "an abdominal tumor." The secretion, which was alkaline and corrosive to the skin, transformed starch into sugar, split neutral fat into fatty acid and glycerin, and digested proteins. Numerous case reports have appeared subsequently, most of which have dealt with pancreatic cysts and acute pancreatitis, in which the loss of pancreatic juice was neither total nor permanent.

When symptoms occurred with such partial or temporary fistulas, they consisted principally of weakness and loss of weight. Cathala and Sénèque reported such a pancreatic fistula which followed operation upon a false cyst of the pancreas after an acute pancreatitis. Marked loss of weight, asthenia, and mental depression were noted, which were considerably ameliorated by reingestion of the pancreatic juice by catheter direct from the fistula. A pancreaticogastrostomy was then performed with complete recovery. It is well to note that the clear fistulous fluid in this case provoked only a slight parietal irritation around the cutaneous orifice. It digested fat, but showed a negative reaction for amylase and trypsin, although it was infected with colon bacillus which sometimes activates trypsinogen. Recently, Kahn and Klein also noted absence of digestion of the tissues around the wound in an extensive study of true pancreatic juice flowing from a fistula following operation upon a pancreatic cyst, and demonstrated that the proteolytic enzyme was present as inactive trypsinogen in such cases.

Instances of pathologically proved complete pancreatic fistula are extremely rare in the literature. After a fairly thorough journalistic survey, we were able to find only one unquestioned example of this type, although we have little doubt that others may have been observed. This case was briefly reported by Kleinschmidt as a pancreatic fistula following a Billroth II-Kroenlein resection of the stomach for a large pyloric ulcer, in which the pancreatic duct was apparently severed in freeing the duodenum from the head of the pancreas. The patient developed marked anorexia, lost 15 kilograms, and showed persistent fatty stools on a mixed diet. A second operation demonstrated the fistula to be total, and full recovery resulted in anastomosing the fistula to an upper loop of jejunum.

As Kleinschmidt states, the diagnosis of pancreatic fistula in most cases does not present any difficulty. If, after such operations as mentioned, a clear secretion is discharged which shows the cutaneous erosion and the digestive properties of pancreatic juice, there is no doubt of the diagnosis. If a permanent fistula remains which defies all conservative efforts at treatment, it is almost certain to be a fistula from Wirsung's duct rather than from

any accessory channel or pancreatic cyst. If the pancreatic secretion is completely lacking in the intestinal canal, as shown by the examination of stool and duodenal contents, one can conclude that the fistula is total.

However, a permanent duct fistula is not necessarily total, cognizance of which is not apparent in the reports of clinical cases. It must be remembered that the accessory duct of Santorini often has a definite opening into the duodenum about 2 centimeters above the ampulla of Vater. Consequently, the symptom-complex resulting from pancreatic fistula will also depend upon the presence or absence of this opening and upon the amount of pancreatic secretion that escapes through it into the intestine. Even a small amount of such leakage into its rightful channel will largely mitigate these symptoms as we have seen in dogs. It is quite probable that such a situation existed in the case reported by Villaret and Justin-Besancon in which an operatively proved fistula of Wirsung's duct opening directly on the wall of the abdomen discharged for 7 months with moderate weight loss as the only symptom noted.

Difficulties in diagnosis may arise, moreover, when the fistulous secretion is not simple pancreatic juice. Duodenal fistulas usually produce marked cutaneous erosion due to the activated trypsin, as well as striking general disturbances, and hence offer no such obstacles. On the other hand, a pancreatobiliary fistula may present a baffling clinical problem which may go unsolved or unsuspected until subsequent operation or postmortem examination reveals the true situation. This is especially the case when the fistulous fluid contains trypsin in its inactive form and produces no erosion of the incision. Popper, who has done considerable work on the presence of pancreatic ferments in bile, observes that the demonstration of trypsin in the bile of inflamed gall bladders is difficult and unreliable, even though increased diastase values give evidence of the presence of pancreatic juice in these cases. The very bile color of the discharge is apt to make one overlook the possibility of other concomitant secretions. Furthermore, the large fatty stools may be incorrectly ascribed to the lack of bile rather than of pancreatic secretion in the intestine. Just such difficulties occurred in our case.

The point we should like to stress is the potential value of the symptomatology as a stimulant to further investigation of persistent or deleterious *biliary* fistulas. Such external biliary fistulas were much more common in the early days of bile tract surgery when cholecystostomy was the operation of choice. No harmful effects from the protracted loss of human bile were noted by the medical authors of that period and this view has been generally held until the present time with but a few exceptions. Early experimental work appeared to show notable effects on dogs from prolonged biliary drainage unless the diet was regulated, but more recent work as noted above (32) indicates the relative innocuity of such fistulas. From the clinical side, Bernays, in 1885, referred to a negress operated upon by Hodgen who had a complete biliary fistula for 11 years with no impairment in health. Balfour and Ross observed 34 cases of prolonged drainage of *all* the bile to the surface with an average duration of 7 months and a maximum duration of 3 years, in none of which were definite recognizable disturbances seen, other than anæmia. Similar instances are too numerous to mention.

Wangensteen, on the contrary, reported 2 cases of external biliary fistula in which there were profound loss of weight and deterioration in strength ascribed to the loss of the bile. He further cited several earlier examples of similar character. Without going into details, examination of each of the above case reports, in which pathological findings are recorded, shows some type of obstruction at or so near to the ampulla of Vater that pancreatic as well as biliary secretion must in all probability have been diverted from the intestine and out through the fistula. A pancreatic carcinoma involving the terminal common bile duct and a gall stone impacted almost in the ampulla with stricture of the papillary orifice were noted to be the obstructing elements in Wangensteen's 2 cases. Willett's case concerned a complete obstruction of the common bile duct, with the production of a biliary fistula following a cholecystotomy. The fluid was noted to

be *colorless*. The patient was lost track of, but "died 9 months later," it is said, "exhausted by sores produced by the discharge." Here is presented circumstantial evidence of the loss of pancreatic principle through the fistula.

In addition to impacted calculus at the ampulla, cicatricial stenosis of the orifice, and carcinoma of the pancreas and bile ducts, the obstruction may of course be caused by any benign or malignant tumor of the papilla itself. The association of a postoperative fistula with just such an entity provided the material for the present case report.

CASE REPORT

H. S. B., white, housewife, aged 61 years, was admitted to the surgical service of Union Memorial Hospital for Dr. John M. T. Finney on September 17, 1932. The patient had enjoyed very good general health until 3 years prior to admission when she suffered a severe attack of epigastric pain radiating through to the back and requiring morphia for relief. The paroxysm was associated with frequent vomiting, clay-colored stools, and slight jaundice for several days.

During the same year, twelve similar spells of increasing severity were endured. In the following 2 years, chills replaced the pain in the attacks. In the 7 weeks before admission, the patient had four chills followed by high fever. Slight weakness and a loss of 30 pounds in weight were also observed over the 2 year period. The patient entered the hospital during an interval period.

The family history was non-contributory. The past history revealed an attack of typhoid fever at the age of 17 years without complications, an occasional attack of tonsillitis, and the extraction of three abscessed teeth the year previous.

Physical examination showed the patient to be well nourished with good color to the mucous membranes and no evident jaundice. The rest of the examination was not remarkable except for slight tenderness and resistance over the gall-bladder region. Blood pressure was 118/74. Urinalysis was negative except for a very faint trace of albumin. No specimen of stool was obtained before operation. A diagnosis of chronic cholecystitis with cholelithiasis was entertained.

Operation on September 19 by Dr. Finney revealed numerous adhesions about the ascending and transverse colon, a long, slender appendix densely adherent in the pelvis, and a thick walled gall bladder containing a single stone. The pancreas, liver, and stomach appeared normal. The adhesions were freed, the appendix removed, and the gall bladder dissected free. The cystic duct was ligated with No. 2 plain catgut and fine silk. One cigarette drain was inserted to the stump of the cystic duct and the abdomen was closed.

The pathological report noted an obliterated appendix lumen and an atrophic, eroded gall-bladder mucosa with marked thickening and fibrosis of wall, and diffuse infiltration with lymphocytes.

For several days following operation, the patient suffered moderate distention, which was relieved by routine procedures. The incision drained only a small amount of serous fluid and on the sixth day after operation the drain was removed. The patient appeared somewhat improved during the next week, except for failure to gain much strength. During this period, there was a tendency to diarrhœa with frequent brown fluid stools containing bile.

On October 1, the thirteenth day after operation, profuse amounts of clear yellow bile colored fluid began draining from the wound. This was followed in several days by very marked and persistent anorexia and nausea, with occasional vomiting and striking weakness. At the same time, the stools were observed to be very bulky, formed, foul-smelling, and clay-colored, with a large quantity of fat microscopically and chemically, and with a negative test for bile. Fluids were maintained by means of repeated infusions of normal saline, and during one 4 day period by continuous intravenous cannula, 5 per cent glucose in normal salt solution being used. Nourishment consisted of such liquid and soft foods as the patient could be encouraged to take.

On the twenty-second day after operation, the patient appeared to slip into a state of complete exhaustion, apathy, and shock with cold moist extremities and an imperceptible pulse. Dr. Walter Baetjer was called into consultation at this time. A blood count revealed a hæmoglobin of 120 per cent and a white count of 32,000. Urine showed no acetone or diacetic acid. Obviously, marked dehydration was present, in spite of the abundance of fluids the patient had been getting the previous week. With the aid of subpectoral infusion of normal saline and intravenous administration of glucose solution and blood, she rallied out of this crisis and 2 days later showed a red blood count of 4.82 million, hæmoglobin of 97, and white blood count of 15,800. In an attempt to relieve and circumvent the extreme anorexia and nausea, a Levine tube was passed, through which the stomach was occasionally washed and the patient fed.

At times the fistulous fluid was cloudy and had a foul odor. A culture taken during one of these periods yielded Bacillus coli.

On October 18, 30 days after operation, a rubber tube was inserted into the fistulous tract and the bile fluid collected in a glass receptacle. Upon appearing clear, this was fed back to the patient through the nasal tube, 300 to 600 cubic centimeters being administered daily until the day before death, although these amounts represented only the major portion of the total daily discharge. This resulted in no abatement in the symptoms, however, and the extreme distaste for food, nausea, occasional vomiting, emaciation, tremendous exhaustion, mental

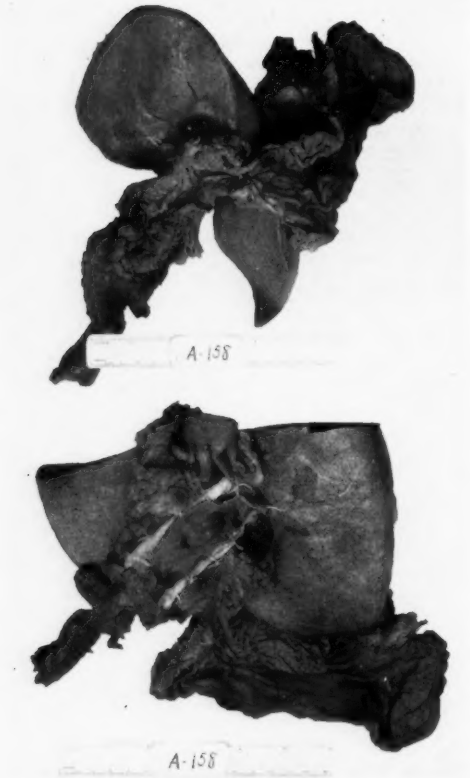

Fig. 1, above. The gross appearance of the papillomatous involvement of the ampulla of Vater. Microscopic examination revealed carcinomatous changes.

Fig. 2. Showing the marked dilatation of the duct system resulting from the obstruction at the ampulla. *a*, Common duct; *b*, stump of cystic duct.

depression, and anhydræmia continued until the end. The weakness and apathy were so striking that the patient made not the slightest voluntary effort and was only moved with great difficulty. Blood chemistry on October 21 revealed non-protein-nitrogen 36.7, sugar 153, and chlorides 201 milligrams per cent.

The patient became irrational at times toward the end and bronchopneumonia finally supervened 48 hours before death, which occurred on October 25, 5 weeks after operation and only 3 weeks from the beginning of the fistula. The temperature, pulse, and respiration showed no significant variations from normal during the entire illness until just before death. The blood-pressure averaged 120/80 throughout except for the one instance mentioned.

The fistulous tract and the skin surrounding the wound at no time showed evidence of erosion. Furthermore, the fluid in its original form had no digestive action on test with meat protein, indicating the absence of active trypsin.

The autopsy findings (by Dr. W. C. Merkel), apart from the operative region, consisted of early bilateral basilar lobular pneumonia, cloudy swelling of the heart, liver, and kidneys, and right sided cardiac dilatation. A bile stained postoperative sinus tract extended from the incision to the floor of the hepatic fossa. The duodenum was opened and a papillomatous growth slightly larger than a pea was seen to occupy the site of the ampulla of Vater with obstruction and compression laterally of the orifice of the common duct. This duct was enormously dilated, measuring 1½ centimeters in diameter, with free passage into the stump of the cystic duct, which communicated with the fistulous tract. No evidence of ligature was encountered. Both hepatic ducts and the main pancreatic duct with its radicals were also markedly dilated. Intensive search for an accessory pancreatic channel into the duodenum was without success. The pancreas and liver appeared normal in the gross. Microscopically, the pancreas showed small areas of interstitial fibrosis and the liver revealed evidence of a very early biliary cirrhosis. Microscopic examination of the ampullar neoplasm disclosed adenocarcinoma arising in an area of papillomatous hyperplasia of the mucosa of the common duct at its orifice (Figs. 1 to 3).

From these findings, it was considered that both the bile and pancreatic secretions were evacuated into the fistulous tract of the operative wound. The marked dilatation of the ducts gave evidence of the resistance to the usual manner of flow and it was believed that the increasing pressure eventually ruptured the stump of the cystic duct.

This case illustrates the point mentioned, that it may be quite a difficult problem to diagnose and treat correctly a complete pancreato-biliary fistula in which there is no erosion of the skin and nothing to suggest the vital loss of pancreatic secretion except the clinical syndrome, if the latter is not recognized. It was felt at the time that the progressive decline without obvious cause represented some type of deficiency disease, most probably of the pancreas, and yet the absence of active trypsin in the fistulous fluid and the apparent lack of any similar clinical picture in the readily available literature left the nature of the condition undetermined until postmortem examination.

Yet, in retrospect, and after an extensive survey of the experimental and clinical literature, we have failed to note any similar case in which this now understood syndrome was so clearly delineated and so analogous to the

deleterious and fatal effects produced by the total loss of pancreatic juice in experimental animals. The microscopic appearance of the pancreas bore a close resemblance to the changes described by Elman and McCaughan in their fistulous dogs.

The pathological lesion at the basis of the complete fistula in this case is rather uncommon, less than two hundred instances of carcinoma of the ampulla of Vater having been noted in the literature.

After witnessing the profoundly deleterious effects resulting from the total exclusion and loss of pancreatic secretion from the intestine, one wonders how large a part the pancreas plays in those types of obstructive jaundice in which both the bile and pancreatic ducts are obstructed and these secretions fail to reach the intestine. Why is carcinoma of the pancreas and especially of the ampulla so rapidly fatal? As Upcott has well remarked, there is probably no portion within the human body outside of the central nervous system where a growth while yet so small is heralded by more widespread symptoms than at the *lower* end of the common bile duct. In over three-fourths of the 110 cases of ampullar carcinoma collected by Outerbridge from the literature, the growth was limited to the papilla and its immediate surroundings, death apparently occurring as a direct result of interference with the flow of the external secretions.

The rapid course with jaundice, loss of weight and strength, and exhaustion death within a period of a month is so dominated by the obstructive jaundice that the obstruction to the pancreatic secretion is apt to be overlooked in explaining the quick exitus. The clinical picture is usually ascribed to the toxic effect of the bile (4), whereas the symptomatology with the exception of the jaundice points as much if not more to an insufficiency of the pancreas in these cases. This suggests to us that the latter factor may be the lethal one in carcinoma of the ampulla and pancreas, and in other tumors and lesions in this region, which act so as to shut off completely from the intestine the pancreatic secretion as well as the biliary principle. Marked obstructive jaundice is frequently seen with little impairment to the general health, as in catarrhal jaundice and stone in the upper part of the common duct. Further investigations are certainly indicated in clearing up this important point.

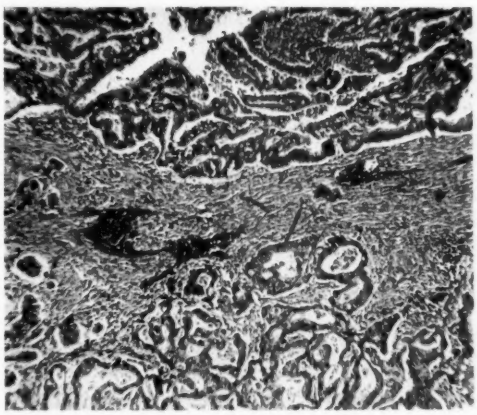

Fig. 3. Low power view showing the transition from papillomatous hyperplasia of the mucosa of the common duct (above) to frank adenocarcinoma (below).

TREATMENT

Space will not permit us to go fully into the treatment of pancreatic fistula, and we shall merely sketch some of the more current therapeutic procedures. Treatment may be conveniently classified into conservative, into which most cases fall, and radical, in which the fistula arises directly from Wirsung's duct in the head of the pancreas in which progressive emaciation and lack of response to conservative measures make operative interference imperative. Wohlgemuth's much quoted regimen consists in suppression of carbohydrate in the diet and the administration of alkali in high dosage, both of which were noted to decrease markedly the amount of pancreatic secretion in a case of fistula on which he carried out extensive therapeutic experiments. According to Pregl, and also Kroiss, ereptone can be employed to advantage by mouth and enema, through which the defect in the diet may be remedied and carbohydrate added. Hartman and Santy have presented good results with atropine and bella donna, alone or associated with Wohlgemuth's diet. Fresh sheep's pancreas is said to be beneficial when fed in daily amounts of at least ¼ pound.

Schmilinsky, in 1912, was the first to report the beneficial effect of feeding back fistula bile and intestinal juice from small intestinal fistulas. Gerster, in this country, came to a similar conclusion, that the administration of bile in physiological amounts is a method for materially improving the condition of debilitated patients with common duct obstruction. Such feeding must be by stomach tube, since the experience of Kausch shows that bile cannot be administered by mouth. Amelioration of symptoms by tube ingestion of fistulous pancreatic juice has also been reported by Cathala and Sénèque as noted above. The general treatment must always include parenteral administration of fluids, dextrose, and chlorides as long as the toxæmia, starvation, and excessive fluid loss by fistula and vomitus persist.

Local treatment has consisted of various astringents, curretage, dilatation, suction pump drainage, and rontgenotherapy. Potter claims striking success by puddling the crater of the wound in gauze soaked in bovinum and feeding 1/10 normal hydrochloric acid to the fistula by a medicine dropper or Murphy drip.

Operative procedures are either designed to extirpate the fistulous tract, if fistula is incomplete, or to anastomose the pancreas or the tract to a hollow viscus, usually the stomach or duodenum. Successful results have been reported with all these types of operations, some of which have been performed as a sequel to a first stage extirpation of a tumor of the ampulla of Vater, such as was present in this case.

SUMMARY

1. It is suggested that complete exclusion of pancreatic juice from the intestine with loss by external fistula produces a highly characteristic clinical syndrome consisting of striking anorexia, nausea, intermittent vomiting, steatorrhœa, extreme exhaustion, anhydræmia, and emaciation, with lethal termination.

2. A clinical example of this symptom-complex is presented, corresponding in all important respects with the deleterious and fatal effects of complete pancreatic fistula in experimental animals.

3. The necessity for totality of the fistula in producing the complete syndrome is stressed, presupposing in every instance a complete obstruction of Wirsung's duct and an absence or obstruction of accessory duct openings into the intestine; hence, the rarity of the condition. It appears that partial or incomplete pancreatic fistula may, in certain instances, be associated with such symptoms as anorexia, weakness, loss of weight, and steatorrhœa.

4. Concomitant biliary principle and absence of trypsin or erosive properties in the fistulous fluid may readily lead to errors in diagnosis.

5. The question is raised as to whether the exclusion of pancreatic juice from the intestine in some types of complete obstructive jaundice may not be the major factor in the rapidly fatal outcome, as for example in carcinoma of the ampulla of Vater and carcinoma of the pancreas

6. A short résumé of the more accepted methods of treatment in pancreatic fistula is presented.

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THE VALUE OF ESTIMATIONS OF THE AMYLASE OF THE BLOOD IN THE DIAGNOSIS OF SUSPECTED PANCREATIC DISEASE

An Experimental Study and Review of the Literature

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THE incidence of disease of the pancreas is probably greater than is generally supposed. Mayo-Robson and Cammidge (1907), Moench (1924), and Barron (1925) noted an incidence of slightly more than 2 per cent of lesions affecting the pancreas. Elman, Arneson, and Graham (1929) found lesions of the pancreas to the extent of 3 per cent in 3,600 necropsies and in the records of 69,000 patients in hospital found an incidence of 0.25 per cent with a diagnosis of pancreatic disease of some type exclusive of diabetes mellitus. Mayo-Robson and Cammidge state that many lesions of the pancreas go unrecognized, the chief reasons being the absence of a syndrome pathognomonic of pancreatic disease, the inaccessibility to palpitatory diagnosis and roentgenography, the lack of a reliable test of function, and finally the rapid autolysis in the pancreas after death.

McWhorter studied 64 case reports of acute pancreatic necrosis by members of the Chicago Surgical Society and found that the correct diagnosis was made only eight times, or 12 per cent. The diagnosis was entirely incorrect in 48 cases, or 75 per cent. A definitely lower mortality was noted in the cases in which operation was performed immediately as compared with those cases in which operation was performed late. McWhorter states "Considerable progress has been made through experimental study and by more general clinical recognition of acute pancreatitis, but owing to its infrequent occurrence and to the relatively difficult diagnosis, little progress has been made in reducing the incidence or in lowering the mortality, of this highly fatal condition."

Schmieden and Sebening, reported 2,137 cases of pancreatic affections of various kinds. In the group with acute pancreatic necrosis, a positive diagnosis was made in only 21.8 per cent of the cases and suspected in 17.5 per cent. These authors likewise state: "In contrast to the rarer general picture of acute pancreatitis, there is still lacking a modern aid for making the exact diagnosis in the numerous atypical cases. Even today we must manage without a pathognomonic test which would make the diagnosis positive."

In practice the diagnosis of pancreatic affections of surgical interest depends almost entirely on physical signs and symptoms which, though fairly characteristic, may readily be confused with other intra-abdominal conditions. Laboratory methods for the detection of disturbances in the function of the pancreas though numerous in the literature have unfortunately been little used in actual practice. Tests for disturbances in the physiology of the pancreas with few exceptions are based upon an investigation of the function of the pancreas with respect to the activity of its enzymes. It is unfortunate that special works on the diagnosis of disease by laboratory methods place too much emphasis on tests of pancreatic function which have been abandoned or which have been shown to possess but little value. The principle, however, of investigating the function of the pancreas by a study of the blood for evidence of an abnormal concentration in its enzyme content, as an indirect index to coincidental pathological changes, is apparently sound but the method should be quantitative rather than qualitative. Such tests when applied to the fæces, the urine or the gastric or duodenal content are more difficult of control and, therefore, less significant than when applied to the blood.

THE BLOOD AMYLASE: A REVIEW OF THE LITERATURE

In 1803 Payen and Persoz precipitated a starch splitting substance from malt and gave it the name of diastase. The diastatic activity of the blood was observed first by Magendie in 1846 who showed that the blood was

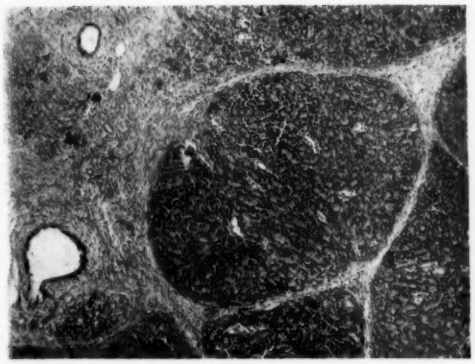

Fig. 1. Low power photomicrograph of pancreas after total occlusion of pancreatic ducts. Shows degree of interacinar and interlobular fibrosis, atrophy of acini and dilatation of ducts with periductal fibrosis.

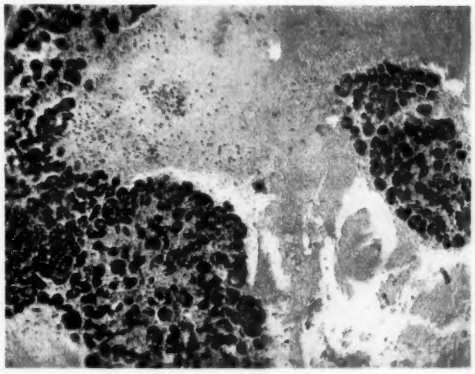

Fig. 2. Low power photomicrograph of pancreas following experimental trauma. This photomicrograph shows the degree of hæmorrhage into the intracinar and interlobular stroma.

capable of splitting starch into sugars. Foster first measured diastase quantitatively in animal organisms in 1867. The next most important contribution to the subject was that by Wohlgemuth (49) who in 1908 described an improved quantitative method for the determination of amylase. Following Wohlgemuth's work, various other quantitative methods were described, most of which depended on the ability of amylase to effect a given change on a known solution of starch. Northrop and Hussey conceived the idea of measuring the viscosity of solutions containing enzymes (trypsin) during the period of action of the enzymes. They found that the change in the initial viscosity of the substance was inversely proportional to the amount of enzyme. Davison employed the technique of Northrop and Hussey to determine diastatic activity, using instead of a 3 per cent gelatin solution, a boiled autoclaved buffered solution of starch two and one-half times more viscous than water and obtained for diastase results similar to those which were obtained by Northrop and Hussey for trypsin and pepsin. Maslow and Davison compared the viscosimetric with other accepted methods, such as the iodometric, the copper reduction and the polariscopic methods, for determination of the activity of diastase and found that the results were similar.

Carlson and Luckhardt called attention to the fact that the body fluids vary considerably in their concentration of diastase, the blood serum having the highest content and the cerebrospinal fluid the least. They came to the conclusion that, in all probability, the amylase was simply a by-product or discard of general tissue metabolism. Bainbridge and Beddard found a diastatic ferment in the livers, muscles, and blood of diabetic patients and depancreatized cats but made no attempt to ascertain whether the amounts were more or less than normal. Milne and Peters obtained decided increases in the diastase of the blood after pancreatectomy in dogs whereas Schlesinger found a diminution or disappearance of amylase in the blood after pancreatectomy and advanced the view that the ferment was mainly of pancreatic origin. This observation was later confirmed by Davis and Ross who likewise found that removal of the pancreas decreased the blood diastase markedly. Carlson and Luckhardt could find no constant difference in the concentration of the diastases in the portal and hepatic serum, and Schlesinger after extirpating the salivary glands could find no significant differences in the blood leaving the pancreas and in the general circulation. Ligation of the pancreatic duct invariably results in an increase in the concentration of the blood amylase (41, 7, 50, 18, 24, 16, 12, 21). Kasahara and Takaishi have also demonstrated increases in

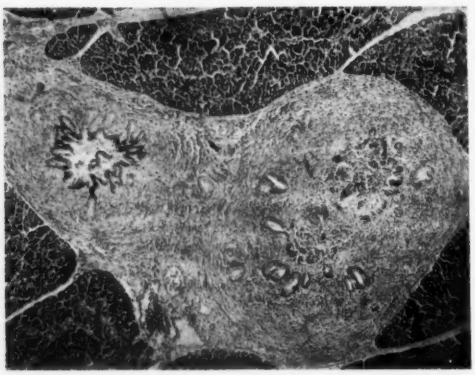

Fig. 3. Low power photomicrograph of pancreas after injection of the larger pancreatic duct with a 5 cubic centimeter suspension Bacillus coli shows intramural œdema and infiltration with polymorphonuclear leucocytes and round cells. There is some disintegration of the mucosal lining and a considerable amount of cellular débris within the lumen of the duct. The acini appear fairly normal.

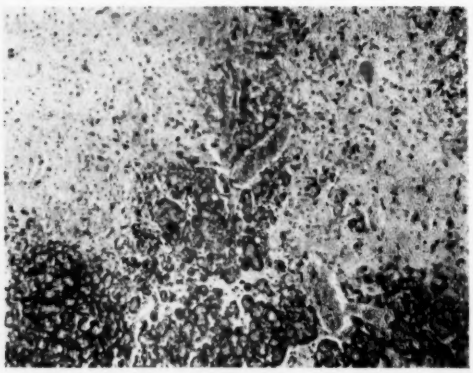

Fig. 4. Low power photomicrograph of pancreas after injection of 15 cubic centimeters bile with rupture of the major pancreatic duct system shows an acute pancreatic necrosis with occasional islands of intact acinar cells.

diastatic ferment in the cerebrospinal fluid following ligation of the pancreatic duct. In experimental injuries to the pancreas, increase in the urinary diastase was noted by Wohlgemuth and Noguchi (52). Of particular interest is an observation by Wohlgemuth (50) that ligature and division of the common bile duct in a series of dogs caused a delayed but considerable secondary rise in the diastatic activity of the blood and urine and a simultaneous fall in the diastase content of the fæces. This did not occur, however, if the upper pancreatic duct was ligated and sufficient time allowed for a stabilization of the diastase concentration of the blood before ligation and division of the common bile duct was performed.

Elman and McCaughan (16), using the viscosimetric method made quantitative determinations of the amylase in the blood of normal dogs. They observed that the amylase of the blood was comparatively uniform in normal animals and that fasting and meals did not seem to have any influence. Ligation of the pancreatic ducts caused marked increases in the amylase content of the blood. In three animals with total external pancreatic fistulæ, they showed that the intestinal absorption of diastase was insignificant in maintaining the level of the enzyme in the blood. Henning and Bach have confirmed this latter result for human beings. Johnson and Wies likewise obtained rises of several hundred per cent in the serum amylase after ligation of the ducts. The level was sustained for variable periods of time usually for 5 to 12 days followed by a decline to within 100 per cent of the preoperative level. No variation in controls was observed where the pancreas was merely exposed. Histologically, they found atrophy of the acinar tissue but the islets were unchanged.

Extensive investigations of the blood amylase in disease have been made. Wohlgemuth (51) reported considerable fluctuation in the amylase concentration of the blood and urine in health but noted marked increases in acute conditions affecting the pancreas. Similar observations have been made by others (20, 25, 29, 19, 24, 39, 42). Benćzur reported marked increases in nephritis but also found considerable variations in the diastase concentration in both blood and urine in normal individuals. The values for blood amylase in normal persons according to many other investigators, however, are fairly constant and unaffected by diet (23, 32, 9, 45, 8, 40). Myers and Killian, using a copper reduction method, found increased diastatic activity of the blood in both diabetes and nephritis. They were unable to offer a satisfactory explanation for the former condition although the latter they stated undoubtedly depends on a decreased excretion of the diastase.

Stocks found an increase in blood amylase in the presence of carcinoma of the pancreas, nephritis, and chronic passive congestion and in some cases of diabetes mellitus. Arneson and Morrin found that pregnancy had no effect on the blood amylase, but that a slight rise was noted in difficult or prolonged labors. In toxæmias with hypertension, blood amylase values were below normal. They found as have others (8, 40,) that urine varies too much for satisfactory estimation.

Somogyi was led to develop another method of studying blood diastase because of the conflicting conclusions in the literature. In healthy humans, he found four-fifths of the diastase in the plasma and only one-fifth in the corpuscles. He noted that the normal diastase content of the blood displayed variations of as much as 100 per cent. In toxæmic conditions, it usually was greatly diminished. Tureen used Somogyi's method in the study of blood diastase in cancer and concluded that as a diagnostic test of cancer, the determination of amylase in the blood was not significant.

Elman (13) studied the blood amylase in pancreatic disease using the viscosimetric method. In 5 patients with pancreatic diseases, variations from the normal value were encountered. In 30 patients suffering from other diseases, the blood amylase was within normal limits. The value of amylase determinations in the blood in subacute and in chronic pancreatic diseases was studied by Wakefield, McCaughan, and McVicar, also using the viscosimetric method. In a group of 20 patients known to have pancreatic tumors, the values for amylase in the blood were increased in 6 and normal in 14. In a group of 30 patients suffering from various other diseases, the values for amylase in the blood were increased in 2 cases. These authors concluded that the percentage of positive results seemed too small to warrant the adoption of a routine diagnostic procedure of study of the amylase of the blood in cases of suspected pancreatic disease. McCaughan (47) obtained experimental data on the dog which suggested that the value of the study of blood amylase as a diagnostic test in pancreatic disease is largely limited by consideration of the time factor. Elman, Arneson, and Graham (15) determined the concentration of amylase in the plasma in 60 adult humans. They believed that they could demonstrate a definite correlation between concentration of blood amylase and the presence or absence of disease in the pancreas, and stated that this supported the experimental evidence that this ferment in the blood is largely of pancreatic origin. Elman (14) collected 20 more cases in which blood amylase was studied. The findings, he stated, indicated that a normal blood amylase was found when the acini of the gland were normal and that deviations from this normal value in the nature either of increases or decreases were noted when the acini or ducts were diseased.

While many other investigators have observed the amylase of the blood of human beings and lower animals, both in health and in disease, the results are far from uniform. Differences in method and the variety of measuring units make satisfactory interpretation of the data of various observers difficult. Nevertheless, it seems generally accepted that the blood amylase is fairly constant under normal conditions and significant variations do occur in the presence of disease of the pancreas. The apparent divergence of opinion as to the clinical value of routine determination of blood amylase in the diagnosis of disease of the pancreas led to the present experimental investigation.

EXPERIMENTAL PROCEDURE

Blood amylase determinations were made on samples of oxalated dog plasma with viscosimeters of the Ostwald pattern as the substrate, a specially buffered and autoclaved solution of starch prepared according to the method of Lintner (Merck) being used. The technique followed was essentially that described in 1927 by Elman and McCaughan and used since with slight modification by Elman and his coworkers and by Wakefield, McCaughan, and McVicar. Healthy dogs of either sex and of approximately similar weight were chosen. They were kept in clean, well ventilated cages and fed a uniform diet consisting of Pratt's dog biscuits and as much

water as desired. The various operative procedures are described below. These were carried out under ether anæsthesia, and a strictly aseptic surgical technique was employed in every instance. The following groups of experiments, which consisted of attempts to reproduce, as nearly as possible, pathological affections of the pancreas encountered in clinical surgery, were performed:

1. A control group: (a) in which the abdomen was merely opened, the pancreas gently handled, and its ducts exposed after which the abdomen was immediately closed: (b) in which the major pancreatic duct was exposed and injected with a sterile solution of physiologic saline.

2. A group in which ligations of one or both of the pancreatic ducts were done. The technique consisted in doubly ligating the duct and dividing it between the ligatures. Omental tags were tucked between the proximal and distal ends of the duct to prevent possible reunion and accessory ducts were carefully searched for in each instance. This group may be subdivided into (a) occlusion of both major and minor pancreatic ducts; (b) occlusion of major pancreatic duct alone; and (c) occlusions of minor pancreatic duct alone. This group was intended to demonstrate the possible effects of ductal obstruction clinically as, for example, by stone, stricture, inflammation, cyst, or tumor on the concentration of the blood amylase.

3. A group in which varying degrees of experimental trauma, simulating pancreatic injury clinically, were produced.

4. A group in which the pancreas was totally extirpated. In these experiments the motive was twofold: first, it seemed desirable to perform pancreatectomy in order to study the general behavior of the blood diastase following its total removal and to compare our results with the observations of Milne and Peters, Schlesinger, and Davis and Ross; and, second, because of the interest which has been aroused by the occasional observation of very low values for blood amylase in patients with extensive malignant infiltration of the pancreas.

5. A group in which various chemical and bacterial irritants were injected into the pancreatic ducts without ligation of the duct following injection and at injection pressures both below and above that required for the injected fluid to rupture the walls of the duct and enter the parenchymal substance of the gland. This group was intended to demonstrate the effects of varying degrees of pancreatitis on the concentration of the blood amylase.

Samples of blood were taken before operation and again at frequent intervals afterward, and an estimate of the amylase concentration was promptly made. At the end of each experiment, the animal was killed unless death had supervened earlier, and a careful necropsy examination was performed. The pancreas was removed and sectioned transversely at four points equidistant along the longitudinal axis of the gland. These sections were stained with hæmotoxylin and eosin and an attempt was made to correlate the anatomical changes with the variations in the curves of the blood amylase.

Results. The following protocols represent typical experiments:

Experiment 1. On January 14, the abdomen of a female dog weighing 12 kilograms was opened and the pancreas gently handled. The major pancreatic duct was exposed in the same manner as in operations for the ligation or injection of the duct and the abdomen was then immediately closed. Thirty-eight days after operation total pancreatectomy was done. The pancreas was grossly and microscopically normal. The blood amylase for the period of observation is shown in Chart I, Curve *1*.

Gentle manipulation of the pancreas during laparotomy produced no change in the level of the blood amylase.

Experiment 2. On January 3, the minor pancreatic duct of a male dog weighing 11 kilograms was doubly ligated and divided. The condition of the animal after operation was excellent. On the fifty-seventh day after operation, the dog was killed under ether and the pancreas removed for study. Grossly and microscopically the gland appeared normal except for slight increase in the connective tissue of the supporting stroma in the cephalic limb. Chart I, Curve *2*.

The least rise in the level of the blood amylase and the smallest degree of pathological change was encountered in ligations of the

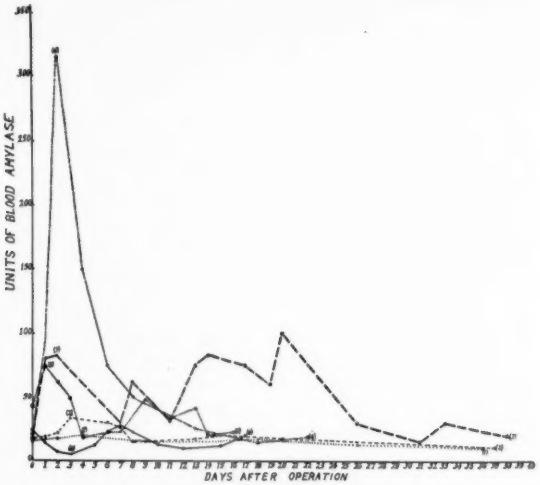

Chart I. Curve *1*, control laparotomy—pancreas gently handled and ducts exposed. Curve *2*, minor pancreatic duct divided between ligatures. Curve *3*, major pancreatic duct divided between ligatures. Curve *4*, major and minor ducts divided between ligatures. Curve *5*, experimental trauma (crushing with forceps). Curve *6*, total pancreatectomy.

smaller upper duct. Apparently the number of acini affected by its occlusion is not great or perhaps adequate anastomoses with the larger lower duct exist whereby the dammed up juice can find its way to the duodenum. The evidence here, however, emphasizes the value of the test, since even minor disturbances are readily demonstrable if the blood be examined shortly after the onset of the obstruction.

Experiment 3. On December 14, the major pancreatic duct of a female dog weighing 11 kilograms was divided between ligatures. Her condition throughout was excellent. Postmortem examination on the thirty-eighth day after the operation showed the pancreas grossly normal but on microscopic examination there was a moderate degree of interlobular and interacinar fibrosis and some atrophy of the acini in the region of the "head" with slight distention of the ducts. Chart I, Curve *3* shows the variations in blood amylase.

Here a somewhat greater rise occurred than in the preceding experiment. The maximum height was attained within the first 48 hours, and fell thereafter gradually toward the preoperative level. This was a common observation in the majority of experiments. This particular experiment was of interest because of the secondary rises in the curve of the blood diastase, a result which occurred several times in our experiments. This finding will be discussed at length further on.

Experiment 4. On December 24, both pancreatic ducts of a male dog weighing 8 kilograms were divided between ligatures. Following this procedure there was gradual loss of weight and strength. Stools, characteristic of pancreatic insufficiency, were noted. Twenty-eight days after operation the animal was killed with ether and the pancreas removed for study. In the gross, the gland was atrophic, firm and markedly sclerosed. The microscopic picture in all of the sections was that of a well advanced interlobular and interacinar fibrosis with atrophy and degeneration of many acini. In sections from the region of the head of the pancreas, the ducts appeared greatly distended and there was considerable fibrosis of their walls. The islets of Langerhans appeared normal. Chart I, Curve *4*, shows the variation in the blood amylase, and Figure 1 is a photomicrograph of a typical section of the pancreas.

As might be expected the greatest rise in the blood amylase occurred when the outflow of pancreatic juice was wholly prevented by the ligation of both upper and lower ducts. Obstruction to either the major or minor

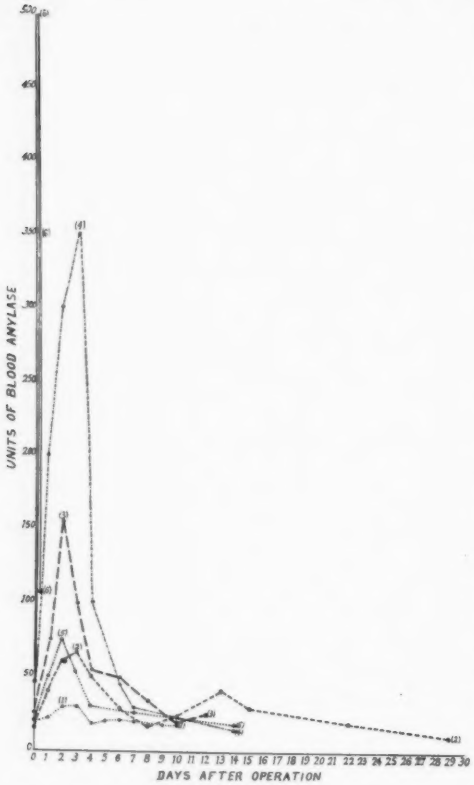

Chart II. Curve *1*, control: injection of greater pancreatic duct with 5 cubic centimeters of sterile saline. Curve *2*, injection of major pancreatic duct with 5 cubic centimeters of gastric juice. Curve *3*, injection of major pancreatic duct with 5 cubic centimeters of bile. Curve *4*, injection of major pancreatic duct with 5 cubic centimeters suspension of bacillus coli. Curve *5*, control: injection of 15 cubic centimeters of sterile physiologic saline with rupture of major duct system. Curve *6*, injection of 15 cubic centimeters of bile with rupture of major duct system.

duct was followed invariably by a lesser degree of elevation of the diastatic concentration of the plasma. The intensity of the pathological changes in the pancreas could be readily correlated with the degree of rise in the level of the blood amylase. Figure 1 is typical of the sclerotic and atrophic changes produced by ligation of both ducts; the effects in experiments in which only one of the ducts was obstructed differed only in being of lesser degree. This group of occlusion experiments indicates the diagnostic value of such observation in human beings when disease of the pancreas is suspected. Calculous, cicatricial, or inflammatory obstructions of the ducts as well as those obstructions arising from compression by tumors and cysts can hardly be differentiated by such studies, but the inference may be drawn that a lesion of the pancreas is present, provided the patient is seen early enough. In general, however, such conditions as enumerated above run a chronic course and are less likely to yield positive results on examination.

Experiment 5. On November 24, the caudad limb of the pancreas of a female dog weighing 8 kilograms was brought out through a small upper right rectus incision and severely crushed with an eight-inch Ochsner hæmostatic forceps; at one point near the major duct the jaws of the forceps were applied to the transverse diameter of the gland several times. There was considerable bleeding within the parenchyma and beneath the peritoneal investment of the pancreas and at several places the pancreas was severely lacerated. The animal remained in excellent condition and 14 days after operation was killed with ether and the pancreas removed for study. Grossly the pancreas appeared normal except for signs of old hæmorrhages beneath the peritoneal covering. Microscopically the principal lesion was a hæmorrhage into the interacinar and interlobular spaces with here and there areas showing atrophy or degeneration of acini. Chart I, Curve *5*, shows the variation in blood amylase and Figure 2 is a photomicrograph of a typical section of this pancreas.

Trauma to the human pancreas, because of its protected location, is a rare occurrence but evidence of pancreatic injury may readily be demonstrated from a study of the blood amylase.

Experiment 6. On March 20, a total pancreatectomy was done on a male dog weighing 12 kilograms. After 5 days, asthenia, polydipsia, polyuria, and loss of weight were evident. The blood sugar by the Folin method ranged from 230 milligrams per 100 cubic centimeters of blood on the second day after operation to 300 milligrams per 100 cubic centimeters of blood on the sixth day after operation. The pancreas was grossly and microscopically normal in appearance. Chart I, Curve *6*, shows the variation in the blood amylase.

Total extirpation of the pancreas causes a rapid fall in the diastatic activity of the blood. This decrease in the amylase concentration, however, is of comparatively short duration and the concentration of the enzyme soon re-

turns to the pre-operative level. This observation would seem to cast some doubt upon the explanations given for the low value of blood diastase reported in patients with carcinoma of the pancreas. Further investigations into the source of blood diastase and into the mechanism by which its concentration in the blood is controlled are desirable.

Experiment 7. On December 5, the major pancreatic duct of a male dog weighing 7 kilograms was injected with 5 cubic centimeters of a sterile solution of physiological saline. The subsequent course was uneventful. Chart II, Curve *1*, shows the variation in the blood amylase. The pancreas was examined at post mortem 14 days later and found to be grossly and microscopically normal.

The slight rise in the curve of the daily blood diastase concentration noted here may perhaps have been caused by the experimental procedure, but such a slight difference in levels of diastase is within the normal range of variability.

Experiment 8. On March 6, 5 cubic centimeters of gastric juice was slowly injected into the major pancreatic duct of a male dog weighing 10 kilograms. There was an immediate change in the region of the injected duct from the normal pink appearance of the parenchymal surface to a deep grayish red discoloration. The animal apparently suffered no ill effects from the injection and on the thirty-second day after operation, he was killed under ether and the pancreas removed for study. Grossly, there was a moderate degree of atrophy and fibrosis; and microscopically, the chief lesions were a periacinar and periductal infiltration of round cells and polymorphonuclear leucocytes. Chart II, Curve *2*, shows the variation in the blood diastase for the period of observation.

The injection of 5 cubic centimeters of gastric juice slowly at low pressure was without effect on the general health of the animal. A prompt rise in blood amylase was the only apparent abnormal reaction to this insult.

The sections from the pancreas at post mortem revealed definite lesions.

Experiment 9. On February 23, 5 cubic centimeters of dog bile was slowly injected into the major pancreatic duct of a male dog weighing 9 kilograms. There was no immediate change in the gross appearance of the gland following injection. Sixteen days after an apparently uneventful course, the animal was killed under ether and the pancreas removed for examination. Grossly, the gland appeared fairly normal but microscopically the larger ducts in the region of the "head" were somewhat distended. There was considerable newly formed fibrous tissue and a moderate degree of round cell infiltration in their walls but the mucosal lining appeared normal. Chart II, Curve *3* shows the variation in blood amylase.

The injection of a small quantity of bile at low pressure had no apparent effect on the general health of the animal. A study of the blood, however, reveals an abnormal rise in the blood amylase and examination of the sections of the pancreas of this animal shows clearly the presence of definite pathological changes.

Experiment 10. On April 10, 5 cubic centimeters of a virulent culture of Bacillus coli was injected into the major pancreatic duct of a male dog weighing 9 kilograms. The animal reacted normally in every way and on the seventh day after operation was killed with ether. The pancreas grossly appeared normal but, histologically, there was distention of the ducts with much newly formed fibrous tissue in the walls and a marked infiltration of round cells and polymorphonuclear leucocytes. There was some desquamation of the ductal mucosa, and, in many instances, the lumina contained considerable amounts of leucocytes and cellular debris. Chart II, Curve *4*, shows the variation in the blood amylase throughout the period.

The injection into the pancreatic duct of suspensions of virulent bacteria without rupturing the duct produced greater rises in blood amylase than occurred in any of the preceding experiments. While there was nothing abnormal in the subsequent behavior of any of these animals it was quite evident from examination of the pancreas microscopically later that definite lesions had been produced. We believe that the evidence indicates that the rise in the concentration of the amylase of the blood is directly due to the effects of experimentation on the pancreas.

Experiment 11. On April 27, 15 cubic centimeters of a sterile solution of physiologic saline was injected into the major pancreatic duct of a male dog weighing 7 kilograms. The postoperative course was uneventful. On the fifteenth day following the operation, the animal was killed with ether and the pancreas removed for examination. It was grossly and microscopically normal. Chart II, Curve *5*, shows the variation in blood diastase.

The injection of 15 cubic centimeters of physiologic saline under sufficient pressure to

rupture the ducts produced a moderate rise in blood diastase but microscopic examination of sections of the pancreas subsequently, revealed no definite evidence of injury.

Experiment 12. On November 18, the major pancreatic duct of a male dog of 10 kilograms was injected with 15 cubic centimeters of bile under sufficient pressure to break through the ducts and force the fluid out into the parenchymal substance. The pancreas quickly became swollen and stained deeply with bile. The animal died early the following morning and at postmortem examination there was considerable thin sanguineous exudate in the peritoneal cavity and a markedly swollen, bile-stained, hæmorrhagic pancreatic gland. There were many areas of fat necroses in the omentum. The major pancreatic duct was probed and found patent. The sections microscopically showed a widespread destruction of all units of the histological structure. Figure 4 is a photomicrograph of a typical area and Chart II, Curve *6*, shows the variations in the blood amylase.

Acute pancreatic necrosis may readily be produced experimentally by the injection of the pancreatic ducts with a larger quantity of fluid and at a pressure great enough to rupture the terminal end chambers of the ducts and thus force the material within the substance of the gland. The course from then on is fulminating and the blood amylase within a very short time increases tremendously. The value of blood diastase determinations in the differential diagnosis of acute abdominal disasters is ably demonstrated in this experiment.

RECAPITULATION

While it is not our purpose to evaluate various methods for the determination of the diastatic activity of the blood, the method used here is probably as satisfactory as any for routine clinical work. We have had no experience with the method recently described by Somogyi but feel that his criticism of one aspect of our method is valid. We too have had the same experience with the difficulty of preparing exactly similar solutions from different batches of starch; this objection in our experience, however, has not been important.

In a series of 15 apparently healthy animals, the amylase of the blood averaged 20.6 units, the lowest reading obtained was 15 units and the highest was 44.4 units.

In experimental pancreatic disease, variations in the level of blood amylase occur with regularity in dogs and definite lesions are readily found subsequently within that organ. On the basis of these experiments, however, it must be admitted that for practical clinical purposes, the value of the study of blood diastase is largely limited by the length of time which has elapsed since the onset of the disease. Experiments which result in obstruction to the outflow of pancreatic juice and experiments which occasion varying degrees of pancreatitis, show rises in blood diastase values above normal within a few hours. The height of the rise seems to be directly proportional to the degree of occlusion of the pancreatic ducts or to the extent of parenchyma involved in inflammatory processes. The maximum rise in complete duct ligation experiments is reached within 72 hours and the curve of increased amylolytic activity is sustained usually for not more than 8 to 15 days. In a few experiments (3 and 5, Chart I, Curves *3* and *5*) secondary rises in amylolytic activity took place after the primary fall had occurred. De Takats and Nathanson made a similar observation during their work on the correlation of the internal and external pancreatic secretions. Using the Wohlgemuth method, they noted an early rise in blood diastase after isolation or ligation of the tail of the pancreas followed by a secondary rise about the seventh day. They make the interesting suggestion that this secondary rise is due to the disappearance of the initial œdema.

While the essential function of the amylase in the various tissues and fluids of the body is not well understood, the mechanism by which increases in the normal content of the amylase of the blood plasma occurs, seems fairly clear. Obstruction of the ducts of the pancreas leads quickly to an overdistention of the ductal system, the back pressure thus caused soon results in atrophy and degeneration of the secreting units, the acini, and further secretion stops; before this stage is reached, however, a reabsorption of the diastatic ferment into the blood stream takes place and its concentration there is greatly increased. The ferment soon appears in increased amount in

the urine and there is a greatly diminished or total absence of diastase in the fæces. Gradually, however, the blood diastase returns to normal concentrations and this recession probably parallels the processes of atrophy and degeneration taking place within the acini of the pancreas. Inflammatory processes also result in abnormally high values, possibly in very much the same way. The inflammatory swelling of the acini and the lining of the ducts is no doubt responsible for the enzymes being passed back into the blood stream and increasing the concentration there far beyond normal. In acute pancreatic necrosis the sudden and extreme elevation in blood amylase is possibly due to the rapid extensive cellular destruction which occurs. The liberated ferments are quickly taken up by the blood and may be found there in great concentration within a few minutes after injection.

Wohlgemuth, and Polacco and Midana have shown, for the salivary glands, that obstruction of Stenson's ducts results in increased diastatic activity of the blood and urine. The salivary glands should be more thoroughly investigated in conjunction with the pancreas. That the pancreas is not the main source of starch-splitting ferments in the blood, is shown by the fact that after total pancreatectomy the blood amylase falls to approximately 20 per cent of the pre-operative level (Chart I, Curve *6*) but very quickly starts back to normal. This return to normal after pancreatectomy occurs in about the same length of time as noted for those experiments resulting in greatly increased concentrations of blood diastase. The reason for this rapid fall in diastase and subsequent return to normal after pancreatectomy is not clear. More study is needed to throw light on the primary source of blood amylase.

In control experiments, gentle manipulations of the pancreas or the injection of 5 cubic centimeters of sterile physiological saline causes no significant variation in the amylase content of the blood. The injection of physiologic saline in amounts of 15 cubic centimeters or more with pressure enough to rupture the ducts caused a moderate rise in blood diastase. This probably is due to mild trauma, as noted by Opie.

Traumatizing the pancreas mechanically also gave rise to a moderate elevation in blood amylase but caused little disturbance in the general health of the animal.

Baló and Ballon studied the effect on the pancreas of obstruction to its ducts. Their observations indicate that acute or chronic retention of pancreatic secretion brings about histological changes consisting of a dilatation of the ducts and end chambers and a flattening of the cells in the glands. Necrosis may then follow and a lipomatosis sometimes results from fat replacement in the necrotic areas. These investigators also believe that an increase in the size of the islands of Langerhans may take place. McWhorter, in a recent review of experimental pancreatitis, notes considerable disagreement among investigators with regard to the readiness with which fatal pancreatitis can be produced. In these investigations, however, the production of acute pancreatitis in the dog experimentally by the injection of bile, gastric juice or virulent bacteria was readily accomplished when care was taken to rupture the pancreatic ducts during injection but if this was not done the effects were mild both clinically and pathologically. The lesions noted in some of our experiments, moreover, are similar to those reported by Johnson and Wies and de Takats. They consist primarily in degenerative changes in the acini and fibrous tissue replacement. Ductal changes pictured by Baló and Ballon were also noted. The islets generally were unaffected. Correlation of the pathological findings with the curves of the blood amylase indicates a direct relationship between the height and the duration of sustention of the curves; and the extent and intensity of the lesions.

CONCLUSION

The normal range of the blood amylase is fairly narrow and is little affected by ordinary conditions of life. Estimations of the blood amylase in suspected pancreatic disease may be of the greatest value; for if increased or diminished concentrations of blood amylase are found, involvement of the pancreas is greatly indicated. The observations, however, must be made during the comparatively

brief period (8 to 15 days) of abnormal blood concentration, otherwise blood amylase values again within the normal range are likely to be encountered. In patients with chronic pancreatitis, pancreatic tumors, cysts and ductal obstructions of various kinds, it would seem, therefore, that many negative results must be expected. Thus the clinical value of the test as a routine will probably not be great except in the few cases seen early by the clinician at the onset of the disease and examined promptly for evidence of abnormal variations in the blood amylase. The technique is simple and the determinations can be made quickly by anyone familiar with the method. This consideration and the fact that a high incidence of positive results may be expected in acute conditions involving the pancreas and that this information would be of infinite value to the surgeon, should recommend this test especially in such cases.

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PRE-OPERATIVE PREPARATION OF THE PERITONEUM IN SURGERY OF THE LARGE INTESTINE

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As the details of the technique of various surgical procedures in the abdomen have become more and more standardized, greater attention has been focused on other factors tending to increase the safety of the operative work. The chief factor in the mortality following operations on the large intestine has been postoperative peritonitis. As we look at the problem as a whole, this postoperative peritonitis is due to one of three causes:

1. Soiling of the peritoneum at the time of operation because of poor technique.

2. Soiling of the peritoneum from a late leak in the suture line. This may be due to poor technique but is more likely to be due to poor pre-operative preparation so that the tissue is in poor condition from œdema. The bowels themselves are in poor condition so that there is abnormal gas pressure after operation and the combination results in poor healing and leakage.

3. A lack of immunity in the peritoneum to a slight infection which, under more favorable circumstances, it should be able to handle.

The first danger has been lessened by the various forms of mechanical apparatus which aid in resections as, for instance, the Rankin clamp and our own intestinal anastomosis clamp (13). The second danger has been lessened by all those measures which improve the condition of the bowel and tend to restore the normal chemistry of the body. The third factor has only recently been studied in an attempt to meet the problem from a practical standpoint.

It has long been recognized that the peritoneum will react to various sterile substances in a manner that is not entirely understood and, up to the present, has been very little studied. The ability of the peritoneum to absorb solutions has been made use of, particularly in children, for the intraperitoneal injection of fluids and for medication. The intraperitoneal use of diphtheria antitoxin has been recognized, the amount of reaction apparently depends on the type of antitoxin used. Where the whole serum was used, there was a marked reaction in 66 per cent of the cases as against 12 per cent where the refined antitoxin was used (7). The peritoneal cavity has also been used for the administration of neo-arsphenamine without harmful effects or damage to the peritoneum (10). Nevertheless, as with every foreign substance, there are reactions in certain cases which are so severe that, at least in experimental animals, a considerable exudate and some later organization have often been demonstrated. Our knowledge of the reaction of the peritoneum to various substances has come because of the need of using this pathway for the introduction of substances either fluid or drugs into the body. Consequently, no other extensive studies of what happens in the peritoneum itself have been made.

Four years ago Rankin and Bargen (8, 9) first published the results of their attempts to immunize the peritoneum by the use of vaccines prepared from streptococcus and colon bacillus recovered from fatal cases of peritonitis. Injections were given intraperitoneally on two occasions before operation with a considerable degree of reaction but with such satisfactory results that the discomfort seemed to be more than overbalanced. They reported a reduction in mortality from 23 per cent to 5 per cent. On the basis of these figures as given, it seems reasonably clear that a local immunity had been produced.

When we use the word "immunity," we are talking about something, the exact nature of which is not understood, certainly not completely. What we actually know about is the result of the process which ends in immunity, and that is the resistance either of the body as a whole or of certain tissues to infection when

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exposed. We have been taught that immunity may be either natural or acquired. Probably all immunity is acquired, although the process in some instances takes place without knowledge or upset to the individual just as it is suggested at present that the so called natural immunity to infantile paralysis may actually be an acquired immunity from an early mild form of the disease too little bothersome to be noticed. As an example of local immunity, we know that in a case of destructive sepsis in a finger where so much damage has been done that amputation is necessary, the safest time to do it is not after the healing has been completed, but before this has taken place when there are certainly some organisms present. To go more directly to the tissue we are discussing, it is a well accepted fact that in a gall-bladder operation following soon after a subsiding acute cholecystitis, pus from the gall-bladder may be spilled into the peritoneum with comparative immunity. Also, in the face of an old fæcal fistula the danger of peritonitis is very much lessened if any operation in the peritoneal cavity has to be undertaken. This is even true after a temporary colostomy has been done to relieve an acute obstruction. The secondary operation necessary to resect a carcinoma has been made much safer because of it.

Also, in considering this question of immunity, certain isolated facts have come to mind which, when put in their proper place, must make us feel more and more strongly that the question of the receptivity of the tissue may be as important as the presence or absence of a small amount of infection. For instance, a few years ago we became interested on the East Surgical Service at the Massachusetts General Hospital in the possibility of infection coming from the inside of a glove torn toward the end of an operation. The bacteriologist at that time was considerably interested and for over 4 months the inside of all of the gloves of the whole surgical team were carefully cultured and it was found that the one man who put the gloves on wet in 70 per cent alcohol would show the occasional culture of a Staphylococcus aureus, streptococcus, or some other organisms as often as the men who used dry gloves. It was found that the house officer in charge of the septic ward was no more likely to have organisms on his hands than anyone else. It was also demonstrated that in none of the cases in which organisms were grown did there happen to be any postoperative sepsis. Recently Hunt has agitated the question of air-born infections and he and others have demonstrated a growth of various potentially virulent organisms on a Petri dish reposing near the open abdominal wound but again no connection between this and fatal infection has developed. In other words, the tissue must be prepared to receive them. This whole problem has been well brought out by Cabot in his article called "The Doctrine of the Prepared Soil."

We must recognize here that factors other than immunity *per se* come into the question because, of course, the bowel above the obstruction has been made more normal and the bacteria present rendered less virile by the other measures used. The tissue has been improved in general condition by relieving congestion and œdema and the chemical balance of the patient has been restored, but certainly no one can deny that the peritoneal irritation which has taken place and the slight peritonitis which has also accompanied the colostomy has added the indefinite something which increases the factor which we call local immunity. In view of all these problems involved in the question of immunity, it is certainly reasonable to employ all the known methods which can be demonstrated to be safe and which may have an effect in lessening the danger of peritonitis in those operations where it is the commonest cause of mortality. Because of the complicated nature of the process we call immunity, it seemed to us that there might be some doubt whether the reaction which came from the use of the vaccine as used by Rankin and Bargen was actually a specific immunization or whether it was in fact merely the response of the peritoneum to an insult represented by the introduction of a foreign protein and whether the same benefits might not come from the same reaction induced with a less marked upset to the patient. Inasmuch as one of us (E.L.Y.)

had been interested in the postoperative use of amniotic fluid and because both from reports and personal use felt convinced that a beneficial reaction took place, it seemed reasonable to believe that the pre-operative use might give the same degree of protective reaction.

In 1927 and 1929 Johnson and Warren published their papers on the use of amniotic fluid in the peritoneal cavity after operation. Since that time, other reports have been forthcoming from Lacey, Trussler, and others (3, 4, 11). It seems clear that there is a certain beneficial reaction in the peritoneum tending to stimulate the normal healing process and as a purely secondary fact, because of this minimizing postoperative adhesions and lessening the tendency toward the development of peritonitis. Experimental attempts to produce peritonitis in control animals have met with considerable difficulty as the animals tend to die promptly from toxic absorption or else to recover without going through the clinical picture of peritonitis as we see it in the human being. Various agents have been used to irritate the peritoneum and, in his studies on peritonitis, David found that a well formed exudate coming as the result of peritoneal injection of 5 per cent turpentine emulsion completely prevented the absorption of Bacillus coli injected into the peritoneal cavity. It seemed to us then that it was reasonable to try the pre-operative injection of amniotic fluid and see if we could demonstrate any beneficial effect from it. The harmlessness of the substance had been already demonstrated beyond question and, therefore, it seemed fair to start at once with clinical cases as well as to attempt to see what actually took place in animals. Accordingly, with the co-operation of the pathological department of the Harvard Medical School and the East Surgical Service at the Massachusetts General Hospital studies were started. There were several problems involved, the first of which was the question whether any peritoneal reaction took place without a constitutional reaction too severe to justify further use. Another was whether one injection or more than one injection was best, and at what time before operation it should be given.

CLINICAL WORK

It is obvious to any surgeon that a great deal of clinical evidence must be available before deductions of value can be made. In this study, we have used pre-operative injections of amniotic concentrate in 49 cases, involving, for the most part, operation on the large intestine. The technique has been as follows: In the first 10 or 12 cases, we used amounts of the fluid varying from 50 to 200 cubic centimeters. We tried using it 1 day, 2 days, and 1 and 3 days before operation. Inasmuch as the result seemed to be the same, we began to use the time interval suggested by the curve of aseptic peritonitis found in experimental animals. Thus, for the last 35 cases at least, the injection has been of 50 or 100 cubic centimeters only, given from 5 to 8 hours before operation. It is given through a small blunt lumbar puncture needle paying due attention to any question of previous adhesions. In one case where there had been multiple abdominal operations we did not use it at all, although we should like to have done so, for fear of injuring bowel as this procedure carries with it the same risk as any abdominal puncture, that of injuring bowels. In fact, that question came up in the only death where postoperative peritonitis was the possible cause. As a rule, there is very little reaction. Several times when the house officer has awakened the patient at three in the morning to give the injection, the patient has gone right to sleep again without discomfort. Nevertheless, in some cases there will be abdominal cramps, nausea, or a little of both, but as a rule, there is not enough disturbance to make the reaction of serious moment to the patient. At the time of operation, if it is done at the height of the reaction, there will be present a cloudy fluid of some 6 or 12 ounces in amount which coagulates very quickly, which is sterile on culture, and has a polynuclear cellular content on smear. The intestines are injected throughout. Even up to 15 hours, the intestines will still be injected and there will be a thin coating of exudate containing mostly polynuclear leucocytes. The patient's leucocyte count taken before the injection and at the height of reaction will increase from normal or slightly above up to 25,000 or even

30,000. The leucocyte count in the peritoneal fluid will be from 50,000 to 100,000. The culture is sterile. Though impressions are deceptive, there is a very strong impression in our minds that the postoperative course in these cases is much smoother than in those cases in which no amniotic fluid was used.

In these 49 cases there have been 3 deaths. All 3 of these have been studied at post mortem and the details are as follows:

One death was shown to be due to postoperative pneumonia and no peritonitis was present.

The second death occurred in a woman of 53 years with an early carcinoma of the sigmoid. A resection and end-to-end anastomosis was done over the Young clamp without difficulty and a cæcostomy was done at the same time. The patient did very well following operation. Her bowels moved on the fifth day by rectum. On the afternoon of the seventh day there suddenly occurred a severe abdominal pain with collapse and evidence of some serious intra-abdominal accident. Patient's condition became very rapidly worse and she died in 24 hours. Autopsy showed a perforation about half-an-inch from the suture line which was undoubtedly due to the cutting of one of the fat tabs with interruption of a terminal artery as described by Rankin. The clinical course up to the time of death and the appearance of the peritoneum at autopsy strongly suggested that there had been no peritonitis up to the time of this perforation.

The third death occurred following a combined abdominoperineal resection for cancer of the rectum. This patient had postoperative intestinal obstruction which required a secondary operation. At the original operation there was localized reddening at one spot on the bowel which the operator thought might have been due to the needle. At the second operation a very slight amount of peritonitis was present and it was impossible to say whether this was merely a congestive change due to the obstruction. However, the patient did have at autopsy a moderate amount of peritonitis. This is the only case in which postoperative peritonitis as such was the cause of death.

If we compare these figures with those for patients who were operated upon at the Massachusetts General Hospital during the same period of time and in whom no preoperative intraperitoneal injection was used, the figures are as follows: 46 cases of large intestinal surgery with 8 deaths from peritonitis, which gives us a mortality of 17.3 per cent. These include many cases in which nothing but a colostomy was done. If we take only those cases in which the bowel was resected, there was a mortality of 38 per cent. Inasmuch as the 49 cases in our series with the injection all include resection, it is fair to use the latter figure of 38 per cent with which our mortality of 2 per cent should be compared. Inasmuch as the type of case is the same and the technique was the same in other respects, it seems that this difference in mortality was not purely accidental.

In one case we used this fluid with the addition of gum tragacanth, as has been recently done in connection with the intraperitoneal use of colon vaccine. Since in this case there was no change in the appearance of the peritoneum, the smear taken did not show any difference in the type of cells and since the technique is somewhat more complicated, we have not repeated the use of this combination.

The results from the cases available up to the present are sufficiently striking to point toward certain conclusions which seem to us to warrant further study along this line. As a matter of fact, they have seemed so suggestive to us that we are using the injection in all such cases as a routine because we believe that the aseptic peritonitis caused by the amniotic fluid lessens the risk of postoperative peritonitis.

EXPERIMENTAL WORK

Investigation of the reaction of the peritoneum to mild irritants, both chemical and bacterial, have shown the occurrence of a cycle of cellular response. Cappell in 1930 demonstrated this by the use of supravalil stains following intraperitoneal injection of guinea pigs with a concentrated infusion broth. He found the first cells to respond were the small mononuclears, followed, during

TABLE I.

Time	Polymorphonuclears per c.mm.
10:00	injection
11:00	occasional
12:00	200– 500
1:00	500–1000
2:00	2200
3:00	5000
4:00	5800
5:00	4900

the initial 18 hours by an increase of polymorphonuclears up to 50 per cent. The maximum reaction occurred between 18 and 24 hours after injection. Repeated injections intensified the reaction, stimulating mononuclear more than the polymorphonuclear cells.

Amniotic fluid concentrate is a very mild peritoneal irritant and the reaction of the peritoneum to its presence was investigated as well as compared to hormone broth and hypertonic glucose solutions.

Guinea pigs weighing about 250 grams were used. The animals received an intraperitoneal injection of 10 cubic centimeters of amniotic fluid through a blunt hypodermic needle introduced slowly through the parietes. Hourly cell counts were then done on the fluid aspirated from the peritoneal cavity through a similar needle. It was necessary to dilute the fluid immediately, since the fibrin present coagulated rapidly. Counts were done hourly during the first 6 hours after injection. A typical chart is shown in Table I.

If a second injection of amniotic fluid were given 24 hours after the first, a more pronounced exudation of cells occurred. It was hard to count the cells accurately because the coagulum formed rapidly. This consisted of fibrin loaded with polymorphonuclears in its meshes. Whereas during the first 6 hours after the first injection the fluid aspirated was clear or only faintly cloudy, that after the second was viscid, yellow, and coagulated rapidly on addition of acid, and showed cell counts varying from 32,000 to 55,000 polymorphonuclears. During this period, the mononuclear cells increased to 30 per cent or more.

Series of counts were done on the fluid after injections of hormone broth and 10 per cent glucose in saline. Cell and fibrin response after the broth was similar to that after amniotic fluid, but was very slight after glucose, usually amounting to a few hundred cells per cubic millimeter with a faint trace of fibrin after treatment with acetic acid.

Guinea pigs receiving 0.5 to 1.0 cubic centimeter intraperitoneally of a saline emulsion of cultures of Bacillus coli from agar slants died very rapidly, usually within 18 hours with little or no peritoneal reaction in the form of vascular infection, cellular exudate, or fibrin deposit. Those animals which received first an intraperitoneal injection of amniotic fluid, followed in 24 hours by equal doses of the saline emulsions of Bacillus coli survived from 36 to 72 hours, and showed a well marked peritonitis with fibrin and exudate. Smears from the peritoneal cavities of the animals without amniotic fluid were found to be loaded with organisms, while the exudate in the injected animals contained many less.

This experimental work is of necessity incomplete. We both came to feel early in the work that the most important thing we could do was to attempt to establish the curve of reaction. This seemed to reach its peak approximately 6 hours after the injection. We depended on the clinical study to give an answer as to the clinical value of this procedure. Further experimental work is being done by others which will tend to help establish the validity of this procedure from the experimental point of view.

SUMMARY

1. A series of cases is here presented in which an attempt has been made to produce a protective reaction in the peritoneum by the use of amniotic fluid concentrate injected before operation. In the series of cases here reported, the mortality was reduced to 2 per cent.

2. A very brief résumé of the experimental work attempting to establish the maximum effect of this injection is given.

3. We believe that the use of this nonspecific peritoneal stimulant contributes materially to the safety of operations in the peritoneal cavity involving resection of the large bowel.

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MALIGNANT DISEASE OF THE FEMALE GENERATIVE ORGANS IN THE FIRST THREE DECADES OF LIFE

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ORDINARILY malignant disease is looked upon as a malady occurring in middle life but it is a known fact to pathologists and gynecologists of large experience that malignancies of the generative organs in childhood and young adult life are, relatively speaking, not uncommon. It is true that with each decade the incidence of cancer increases and that certain types, such as uterine and breast malignancies, occur chiefly in the fourth and fifth decades.

Williams states that the incidence of cancer increases with each decade after 25, rising until the seventh decade, and that females are more precocious from the start as is especially noticeable in the age period 45 to 55.

Observation of malignancy in young adults during the past few years prompted us to review our records and if possible to determine any facts of importance in relation to symptoms, the stage of the disease at the time of admission, treatment, and the results of treatment given.

The experience of all who treat malignancy has been that the disease is virulent in young adults, running a much more rapid course than in patients of middle or old age.

The campaign by various societies for the control of cancer is being carried on more vigorously of late than ever before. This education of the lay people presents the family physician and surgeon with a greater responsibility than ever before in detecting these lesions at the earliest possible moment so that proper and energetic treatment can be instituted.

The yearly or birthday examination will be of benefit in detecting more early cases, but much greater stress must be laid upon the significance of the presence of sores, abnormal discharges, tumor formation, and other symptoms such as pain and pressure, and the fact that cancer is a possibility in childhood and young adult life.

There were 2,405 patients suffering from malignant disease of the female generative organs admitted to the State Institute for the Study of Malignant Disease up to October 1, 1933. We were somewhat astonished to find 114 of these patients were 30 years of age or younger; 4.6 per cent of the total gynecological malignancies admitted. Table I shows the incidence in each group.

TABLE I.—INCIDENCE

Pathology and location of lesion	Total admissions	No. patients age 30 or younger	Per cent of total
Cervix			
Epithelioma	1583	78	4.9
Sarcoma	2	..	....
Malignant polyp	3	..	....
Adenocarcinoma	60	1	1.6
Adenocarcinoma and epithelioma	21	1	4.7
Ovary			
Papillary cyst adenocarcinoma	73	6	8.2
Adenocarcinoma	32	6	18.7
Carcinoma	104	9	8.6
Sarcoma	3	1	33.3
Malignant teratoma	3	1	33.3
Uterus			
Adenocarcinoma and carcinoma	291	1	0.3
Malignant leiomyoma	20	2	10.0
Sarcoma	2	..	....
Chorionic epithelioma	1	1	....
Vagina			
Adenocarcinoma	6	..	....
Epithelioma	80	3	3.7
Sarcoma (botryoides)	1	1	....
Vulva			
Adenocarcinoma	3	..	....
Epithelioma	117	3	2.5
	2405	114	

CERVIX

Cancer of the cervix uteri in young women constitutes 68 per cent of the 114 cases presented here, or 4.9 per cent of the total number of cervix epitheliomata admitted.

Careful inquiry into the histories of these cases revealed: (1) that only one of the 78 patients was unmarried; (2) the 77 other patients had from one to eight pregnancies, bearing out the theory that trauma and inflammatory lesions have a large influence in the production of malignancy of the cervix;

TABLE II.—DURATION OF SYMPTOMS

Group	Shortest duration	Longest duration	Average duration
I	1 month	3 years 8 months	9 months
II	3 months	1 year	6.3 months
III	2 weeks	3 years	7.8 months
IV	4 days	4 years	8.2 months
V	2 weeks	1 year	8.4 months

(3) that all gave a history of discharge, so called leucorrhœa, for varying periods of time up to 7 years; (4) that the important symptoms referrable to menstrual periods consisted of bloody, watery, or foul discharge between the regular periods (see Table IV for age incidence).

In comparing the symptom of discharge in the various stages of advancement little could be learned. In recording the 78 cases of epithelioma of the cervix, the Schmitz grouping was used. Ten cases fell into group I, 4 into group II, 29 into group III, 27 into group IV, and 8 into group V.

Table II shows a comparison of the duration of the symptoms, bloody or watery discharge (leucorrhœa not included) in the different groups. It will be seen that there is little difference of duration in the early and far advanced cases, so not much knowledge is gained to guide us in the early symptomatology.

Blood as a symptom must be looked upon as accidental—yellowish, watery, or foul smelling discharge usually precedes the showing of blood which does not occur until the tumor begins to ulcerate and break down. Abnormal discharges in young women are indications of pathology which usually is found to be endocervicitis with so called erosion. This condition may be considered a precursor to malignancy according to Ewing who says: "A chronic endocervicitis precedes cancer in the great majority of cases and the routine examination of this tissue reveals abnormalities in the morphology and position of the epithelium which constitutes precancerous conditions."

Bailey, in a monumental piece of research "An Inquiry into the Basic Cause and Nature of Cervical Cancer" which is exceedingly illuminating and worthy of careful consideration by all who are endeavoring to prevent malignancy of the cervix, also states that the ultimate sequel to erosion is malignancy.

It will be found that cancer prevention in this particular group of malignancy lies within the grasp of the family physician who should acquaint himself with the evidences of cervicitis, ulcerations, erosions, and leucoplacic areas on the cervix, so that he may advise proper treatment for these precursors of malignancy.

If seen early there is a good possibility of eradicating cervical cancer. The recognition of the disease in its early stage, especially in young women, is important as it may be the means of saving the life of a young mother so needed for her children's sake.

Attention is frequently called to the fact that the incidence of cervical cancer is lower in Jewesses. Sorsby says: "The observance of the Mosaic code undoubtedly produces a high degree of sexual cleanliness; and it is suggested that this cleanliness, with its concomitant restrictions on cohabitation at times when rest is probably beneficial, as after parturition and menstruation, is a factor in the lower incidence of uterine cancer among Jewish women—the regulations of the Mosaic code make the appearance of discharges a cause for inquiry as to its nature, and a woman with a blood-stained discharge is theologically 'unclean'." None of the patients in our group was Jewish.

Parabuceu, quoted by Stout, collected data from several Russian gynecological clinics which show that cancer of the uterus in women from 24 to 30 represents no less than 24 per cent of all cases of uterine cancer. He attributes this to the increasing use of artificial abortion and anticonceptional methods in Russia.

The results of treatment given in this group of patients have been as good as the general average in cancer of the cervix in groups I and II. Group I yielded a 50 per cent 5 year cure in the 6 cases in which the patients were admitted and treated 5 or more years ago. Only one patient in this group died from the disease; the 2 others were lost trace of a few months after treatment and we have been unable to ascertain the end-result so that this 50 per cent is the absolute 5 year cure. Of the

TABLE III.—AGE INCIDENCE—OVARY

Pathological group	10–15 years	16–20 years	21–25 years	26–30 years
Papillary cyst adenocarcinoma				6
Adenocarcinoma		2	2	2
Carcinoma	2	1	5	1
Sarcoma				1
Malignant teratoma			1	

The youngest patient was 11 years of age (carcinoma).

TABLE IV.—AGE INCIDENCE—EPITHELIOMA CERVIX

Age	18	20	22	23	24	25	26	27	28	29	30	Total
Group I						2	1		5	1	1	10
Group II				1	1			1	1			4
Group III			1		3		1	4	6	4	10	29
Group IV	1	1	1	2	1	1	1	3	5	5	6	27
Group V				1	2			1	1	1	2	8
Total	1	1	2	4	7	3	3	9	18	11	19	78

4 patients admitted and treated less than 5 years ago, 2 are clinically well for 11 months each, or since the time of their original treatment, 1 has not returned since treatment and we have been unable to ascertain the result of treatment, and 1 died 4 years after admission from recurrence and extension of the disease.

The group II cases yielded a 33 per cent 5 year cure in the 3 cases with admission and treatment 5 or more years ago. One other patient in this group, admitted 10 months ago, is alive and free from the disease since the time of original treatment.

In the groups III, IV, and V cases, palliations only were rendered; none survived the 5 year period. This is very discouraging in comparison with the general statistics.

Thirteen of the group III cases were admitted 5 or more years ago; all died—8 in less than a year, 2 between 1 and 2 years, 2 between 2 and 3 years, and 1 in 4 years and 8 months. This last patient was clinically well for almost 2 years following her original treatment but had a recurrence which progressed and caused death. Of the 16 other patients, admitted less than 5 years ago—5 are clinically well from 4 months to 13 months; 2 are having palliation for 5 months each; 1 is progressively worse after 6 months; in 1, living 1 year 5 months after admission, the local lesion is clinically well but there are metastases in the abdominal lymph nodes; 1 living 2 years 9 months, was clinically well for 2 years when there was a recurrence which was retreated and she is again well for 8 months; 1 was lost trace of after being clinically well for 4 months; 5 died—4 in less than a year and 1 in 1 year 2 months.

Sixteen of the group IV cases were admitted 5 or more years ago; 10 died in less than a year; 2 in 1 to 2 years; and 4 were lost trace of, unimproved, in from 4 months to 1 year 8 months. The 11 others, admitted less than 5 years ago, also died—8 in less than a year, and 3 in 1 to 2 years.

Of the 8 cases in group V, 1 was not treated, 1 was lost trace of in 7 months, 4 died in less than a year, and 2 in 1 to 2 years.

One case of adenocarcinoma of the cervical canal aged 27 years, and 1 case of adenocarcinoma and epithelioma of the cervical canal aged 29 years, were treated. This latter case had recurred after operation, and at the time of admission both were far advanced. Following irradiation, 1 was lost in 2 months and the other succumbed to the disease in 6 months.

OVARY

Ewing, in speaking of malignant disease of the ovary, says: "All ages are susceptible from birth to senility" and that all lesions, with few exceptions, are very malignant.

We have 23 cases of malignancy of the ovary occurring in patients 30 years of age or younger, to report; 6 papillary cystadenocarcinomata, 6 adenocarcinomata, 9 carcinomata, 1 sarcoma, and 1 malignant teratoma.

Thirteen of the 23 patients were unmarried; 2 of the married patients had no pregnancies; 4, one pregnancy; 2, two pregnancies; 1, three pregnancies; and 1, four pregnancies.

The age incidence in each pathological group is shown in Table III.

Of the 23 cases, only 2 were not proved pathologically; 1 had no operation and the other had had a laparotomy but no section taken. The majority of these patients had been operated upon before admission. One patient was not treated, the others received

either high voltage X-ray or 4 gram radium pack treatment. Six of the patients have lived from 5 months to 8 years after treatment and have been free from the disease for 5 months, 6 months, 2 years 2 months, 2 years 8 months, 2 years 10 months, and 4 years, respectively. This latter patient is alive 8 years since the time of admission but suffered a recurrence 4 years 4 months after original treatment and then was operated upon and treated again. Three others are living but are not free from the disease; 2 for over a year with some palliation, and 1 for 2 months unimproved. Three were lost trace of and the other 10 died—7 in less than a year, 2 in 1 to 2 years, and 1 in 5 years 11 months.

UTERUS

One case of adenocarcinoma of the uterus, patient aged 30 years, was admitted in September, 1930, following curettage. Upon admission she was treated with radium and high voltage X-ray. This patient reported only once following treatment and then was lost, so that the result of treatment was undetermined.

Two cases of malignant leiomyoma were recorded: 1 occurred in a patient aged 24 years, married, menstrual periods from the age of 14 were regular but rather profuse, lasting from 7 to 8 days. She had had one miscarriage but no other pregnancies. Seven weeks before admission menstrual periods became longer and harder. Hysterectomy was performed for a supposed fibroid uterus. Pathological examination showed this tumor to be a malignant leiomyoma. She received high voltage X-ray treatments 1 month following operation and was alive without recurrence 5 years and 7 months after treatment when last examined.

The other case occurred in a patient aged 24 years, married, 6 children. This woman had given birth to a child 6 months previous to admission following which she had a 9 day hæmorrhage. Four months after the birth of the child, a hysterectomy was performed for a malignant leiomyoma. At the time of admission there was a recurrence in the vault of the vagina extending into the broad ligament areas. She was treated by radium applications but the lesions progressed and she died without any palliation 8 months later. Autopsy showed recurrence in the pelvis and generalized metastases.

One case of chorionic epithelioma was observed in a patient aged 30 years, married, a mother of 2 children ages 8 and 5 years. Her menstrual periods from the age of 12 were always irregular. At the age of 29, she began to have a yellowish discharge, and for 3 months previous to admission she had continual bleeding following a miscarriage. A panhysterectomy was performed and sections from the body of the uterus showed the presence of a chorionic epithelioma. Postoperative irradiation given, alive and well 14 years since admission.

VAGINA

Three cases of epithelioma of the vagina were observed; 2 in patients aged 30, and 1 in a patient aged 28.

One patient, aged 30, admitted October, 1932, gave a history of bearing down pain for 7 months, last menstrual period in July, 1932. She was 3 months pregnant at the time her family doctor excised a growth, section of which showed it to be an epithelioma. There was a recurrence of this lesion within a month. Upon admission, the recurring tumor was implanted with gold seeds of radium emanation for a total dosage of 1,363 millicurie hours, following which there was a prompt regression of the tumor. The pregnancy proceeded uninterrupted to full term when a healthy child was born April 14, 1933. On last examination, December, 1933, there was no evidence of recurrence, 14 months. This case typifies the necessity of prompt and accurate treatment, which in this case, was successfully performed; and was not only the means of saving the life of a mother up to the present time, but also the life of a child, conceived before radiation treatment.

One was in a syphilitic, aged 28 years, who gave a history of continuous bloody discharge only, over a period of 2 months. The lesion was far advanced and involved the anterior and lateral walls of the vagina. She was treated by irradiation which proved of little benefit, and succumbed to the disease 9 months after admission.

The other also was a far advanced case. This patient's periods were irregular, occurring every 2 weeks, and she complained of a yellowish discharge between her supposed menstrual periods. At the time of examination there was a large infiltrating growth involving the posterior wall of the vagina and extending into the posterior fornix. She was treated by irradiation but succumbed to the disease in 2 months.

In the case of a child 2 years of age, about 6 months prior to admission, mother had noticed a swelling in the lower abdomen but the child complained of no pain. Following this a growth was found protruding from the vagina and involving the vulva. Part of this was removed by her family physician. At the time of examination here, there was a tumor mass in the lower abdomen extending to the umbilicus and a purulent discharge from the vagina. There was a fungating tumor mass involving the vagina and vulva. Sections from this growth showed it to be myxofibrosarcoma, or sarcoma botryoides. The child died of the disease in spite of irradiation treatment, 4 months after treatment was administered and 10 months from the beginning of symptoms.

Ewing says, "Rhabdomyoma uteri appears almost exclusively as an element in the polypoid vaginal sarcoma of children and adults (sarcoma botryoides, Pfannenstiel). This process affects the vagina in children and chiefly the cervix in adults (Gow and Pick). The symptoms are hæmorrhage, fetid discharge, and protrusion of a polypoid tumor from the vagina, with dysuria, pain, fever, and cachexia. The vagina is eventually filled with ulcerating masses and there are bulky extensions into the pelvis. . . . The usual histology is that of a large spindle cell sarcoma, with many blood and lymph vessels, myxomatous tendencies, and areas of striated muscle."

VULVA

Three cases of epithelioma of the vulva were observed—1 in a patient aged 25 years and 2 in patients aged 30 years.

The patient aged 25 years was single and gave a history of having a small nodule which occurred in the clitoris 1 year prior to admission. At the time of examination there was an exceedingly painful, ulcerating tumor about 3 centimeters in diameter which involved the region of the clitoris and there were palpable inguinal and femoral nodes. The lesion was treated by irradiation with temporary improvement. During the course of 1 year the disease progressed, and she finally succumbed to extensive involvement of the whole vulva and inguinal lymph nodes. In this particular case the use of strong douches of bichloride of mercury may have been an etiological factor.

One of the patients aged 30 years was married. Ten months before admission she noticed a small sore on the labia. She consulted a physician who told her it was an ingrown hair and removed it. As she did not get any relief, she consulted another physician but with no better results. Later as she was 5 months pregnant she went to still another physician who told her the sore would probaby improve after childbirth. At the time of admission the baby was 8 weeks old and the soreness had increased. Examination showed an ulcerating, infiltrating epithelioma involving the whole vulva and clitoris region and large metastatic nodes in both groins. Irradiation in this case was of little or no avail and she died in 4 months. Here, included in this history, is evidence of neglect on the part of the physician to render prompt and efficient treatment.

The other patient aged 30 years was single, the lesion had recurred after operation and was far advanced at the time of admission. It was ulcerated and involved the whole vulva. The treatment was irradiation for palliative effect but she died in 6 months.

CONCLUSIONS

1. Of the 2,405 gynecological malignancies admitted to the State Institute, 114, or 4.6 per cent, occurred in the first three decades of life.

2. Epithelioma of the cervix, in this group of patients aged 30 or younger, is the most common gynecological malignancy; and represents 4.9 per cent of all cervical cancer.

3. Malignancy of the ovary occurring in this age period, represents 10.6 per cent of all

malignant tumors of the ovary admitted to the Institute.

4. Malignancy of the fundus of the uterus, vagina, and vulva occurs much less frequently.

5. Cervical cancer in groups I and II has yielded healings in about the same proportion as the general average in cancer of the cervix, namely 50 and 33 per cent. Groups III and IV and V have been only palliative.

6. One case of epithelioma of the vagina which occurred in a patient 4 months pregnant and which was treated by irradiation, is herein reported. A normal healthy child was born and there is no recurrence after 14 months.

7. This statistical paper was compiled for the sole purpose of calling attention to the frequency of malignant disease of the female generative organs at the early age of 30 years or less.

8. Our only hope of discovering and treating early lesions of the cervix lies in careful gynecological examination bimanually and with a speculum, resorting to biopsy and cauterization in the so called cervicitis and erosion to rule out or discover early malignancy.

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DIAL–URETHANE FOR OBSTETRICAL ANALGESIA

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THE utilization of volatile anæsthetics by Sir George Simpson abroad and Walter Channing in this country constituted an advance, the importance of which can scarcely be overestimated. Improvements in the quality of chloroform and ether, together with the introduction of nitrous oxide and ethylene as anæsthetic agents, marked still further progress in the effort to lessen or abolish the pains of labor. Obviously, however, there are technical difficulties attending the use of any of the volatile anæsthetics in obstetrics; this being especially true as regards nitrous oxide and ethylene, where cumbersome apparatus and the necessity for constant attention by a trained anæsthetist practically limit their administration to the well-to-do, hospitalized patient. Then, too, one should not lose sight of the fact that the possibility of injury to hepatic and renal cells is increased in pregnancy and that inhalation anæsthesia, certainly with ether or chloroform, is contra-indicated in the existence of respiratory tract infection. The ether-oil mixture of Gwathmey, though somewhat simpler to administer, shares all the other disadvantages of ether by inhalation, and, moreover, must usually be supplemented by inhalation anæsthesia in the later stages of labor.

Morphine, the most valuable of the analgesics, is certainly capable of relieving labor pains if given in sufficiently large dose, either alone or in conjunction with scopolamine. That there is definite danger to the child when such doses of morphine are administered to the mother within 5 to 6 hours of delivery has long been known; with growing recognition that both first and second stages of labor may be unduly short, the belief has become stronger and stronger that morphine should not be used during labor, except in small dosage, chiefly as an adjunct to some other narcotic drug. The careful observations of Irving, Berman, and Nelson have led these authors to conclude that morphine or any of its derivatives has no place during labor as they distinctly delay the initial respirations of the child.

Following their employment as surgical anæsthetics, various barbituric acid derivatives have been utilized for inducing obstetrical analgesia. In Europe, pernocton (secondary butyl-beta-bromallyl barbiturate) and, more recently, evipan (methyl-cyclo-hexenyl-methyl-malonyl ureid) appear to enjoy the greatest popularity; while, in this country, amytal (iso-amyl-ethyl barbiturate) has been most used, although some American authors have reported on pernocton and pentobarbital (ethyl-methylbutyl-barbiturate) as obstetrical analgesics. With none of these save amytal have I had personal experience; as to this drug, both from my own observations, as well as from the reports of others, I am quite definitely of the opinion that, while useful in many cases, it is far from being the ideal obstetrical analgesic. Especially objectionable is the marked restlessness noted in a large proportion of the patients given amytal, a disadvantage apparently accompanying the use of pernocton and pentobarbital (6).

My interest in another barbiturate, dial (diallyl-barbiturate), was first aroused by the favorable report of Nelson on its use in obstetrics. This drug has long been used as a hypnotic; acting, according to the investigations of Keeser and Keeser on basal ganglia rather than on the cerebral cortex. Dial is much more active than the chemically related barbital, and recovery from its effects occurs more rapidly; on the other hand, its action is more persistent than that of pentobarbital and, probably, pernocton and amytal. Dial was employed as an obstetrical analgesic by Hussy as far back as 1916; subsequent use of it for this purpose having been made by Krafft and Baumann and Rossier. These early observers administered only small doses of dial orally, however, and the results they obtained should, in all probability, be ascribed to other drugs such as dionine or heroin and chloretone, administered simultaneously.

Dial, itself, is only slightly soluble in water, but an aqueous solution may be prepared from a mixture of dial, urethane, and mono-ethyl-urea. Advantage is taken of this fact in making the ampul solution, which is frequently referred to merely as "dial," but, which, obviously, should be designated as "dial-urethane," because the latter drug undoubtedly contributes to the effects noted after administration of the solution. The mono-ethyl-urea is stated to have no hypnotic action. McNeile, of Los Angeles, was, apparently, the first to use this solution in obstetrics. In his preliminary work he injected 2 cubic centimeters of the solution (containing 3 grains dial and 12 grains urethane) intramuscularly; repeating this dose in only a few instances. He stresses the importance of making the injection at least 1½ inches into the muscle; otherwise, owing to the hypertonicity of the solution, severe local tissue damage will occur. With the dosage and method of administration employed, distinct relief from pain was secured in only a few of his cases, but he expressed the view that a smaller amount of ether, gas, or ether-oil was required by patients who had previously received dial and urethane solution. He was especially struck by the apparent stimulation of uterine contractions and the rapidity with which cervical relaxation took place. Later, he recommended the substitution of the dial-urethane solution for magnesium sulphate-morphine in the Gwathmey technique. Lynch, also, used the dial-urethane solution in this manner with good results.

Garcia, apparently, was the first to administer the dial-urethane solution intravenously in adequate dosage for obstetrical analgesia. Utilizing the "biological" criterion subsequently suggested by Holtermann for evipan; that is, slowly injecting the solution into the vein until the patient no longer responded to questions, Garcia reports very good results in the small series of 11 patients. The volume of the solution used varied from 4 to 7.5 cubic centimeters; a single injection being made.

Nelson, whose paper has already been mentioned, has had a much more extensive experience with the dial-urethane solution in obstetrics, using it in a series of 110 patients, with results that "have been so uniformly satisfactory that I am prompted to report in some detail the effects obtained from this valuable drug." Nelson advocated an initial injection of 2 cubic centimeters of the solution into an arm vein as soon as labor was established. In from 30 minutes to an hour and a half, depending on the rapidity of labor and force of the pains, a second similar injection was given. Four cubic centimeters suffice in some cases; more often, a third injection must be made, approximately half an hour before termination of the second stage. In two unusually large patients with prolonged labor due to posterior presentation, a fourth injection was required. Nelson was able to perform "many difficult procedures, such as forceps, versions, and extractions, episiotomies, and necessary repair without the necessity of additional anæsthetic."

The dial-urethane solution is marketed in 2 cubic centimeter ampuls, in which form it is said to be stable for an indefinite period of time. In using it, I first followed the technique suggested by Nelson, preferring intravenous injection both because much prompter action is secured thereby and also because, owing to its hypertonicity, even intramuscular injection of the solution causes a certain amount of discomfort. With Nelson's dosage, excellent results were secured in some cases, as illustrated by the following brief reports.

CASE 1. Primipara, aged 21 years. At 1:30 p.m. 2 cubic centimeters of dial-urethane solution was injected into the median basilic vein, as definite labor pains had just commenced. The patient was only partially relieved, so 20 minutes later, a second injection of 2 cubic centimeters was given. Following this the patient fell asleep, moaning slightly with each pain. At 6:00 p.m. she was roused and took a glass of water and a bowl of soup; following which a third injection of 2 cubic centimeters was given. Spontaneous delivery occurred at 11:30 p.m. Patient slept quietly all night and was wakened for breakfast at 7:00 the next morning, when she took food with relish. She had no recollection of events from the time of the second injection until she was awakened the next morning for breakfast.

CASE 2. Primipara, aged 19 years. At onset of labor, she was given 2 cubic centimeters of dial-urethane solution in vein. Although partially asleep, she was evidently experiencing considerable pain. Therefore a second injection of 2 cubic centimeters was given 30 minutes later, and this was followed by

complete relaxation and apparent comfort. Uterine contractions occurred strongly and at frequent intervals. The second stage was completed without laceration and any additional anæsthesia. I believe that episiotomy could have been done on this patient without inhalation anæsthesia.

Satisfactory as was the course of labor in cases such as these, instances were encountered in which there seemed to exist a refractoriness to the dial-urethane. This is shown in the following.

CASE 3. Primipara, aged 25 years. Labor was quite well advanced when she was admitted to the hospital; first stage was almost completed. An injection, 2 cubic centimeters of the dial-urethane solution was given intravenously practically without effect. In 30 minutes, a second injection of 2 cubic centimeters was given, with no definite effect. Recourse to inhalation anæsthesia was necessary. A second degree perineal laceration was sustained.

Although unfamiliar with the work of Garcia or Holtermann at the time, it was obvious to me that more elasticity in dosage should be employed, in order to secure satisfactory results in these resistant cases. Dial-urethane, in contrast to barbital, produces its effects very soon, almost immediately after entrance into the blood stream. By making the injections very slowly (about 1 cubic centimeter per minute; never more rapidly) it is possible to adjust the dosage to the individual patient much more accurately than by a fixed volume-dose, as used by Nelson.

TECHNIQUE

The procedure which I now follow is as follows:

The patient is told that she will feel relaxed and sleepy from the injection; a matter of some importance, because, otherwise, alarm may be experienced over the peculiar sensation. Four cubic centimeters of the solution are drawn up into a 5 cubic centimeter syringe and the needle thrust through the vein wall. Injection is made slowly, the patient being constantly questioned, and the injection discontinued when she no longer responds. In some cases, 2 cubic centimeters of the solution will suffice; in others, it may be necessary to inject the full 4 cubic centimeters; I have never given in excess of this latter amount in any single injection. If sound sleep does not occur between pain, a second injection of 2 cubic centimeters is given in 30 minutes. Further injections, each of 2 cubic centimeters, may be given, but I have not exceeded a total of 8 cubic centimeters in the course of any labor.

I have now used the dial-urethane solution in 56 patients and am definitely convinced that, used according to the method just described, it is the most satisfactory obstetrical analgesic I have ever employed.

As to the safety of dial-urethane intravenously in the manner described, far-reaching conclusions can scarcely be drawn from the limited number of cases I have observed. It is worthy of note, however, that Nelson, too, in his series of 110 cases, records no undesirable side-actions, and that Marney, in a series as large and with a dosage 50 per cent greater, concludes that the preparation is "perfectly safe."

The following two cases are especially interesting.

CASE 4. Multipara, aged 36 years; in the ninth month of pregnancy. She was toxic; urine albumin, 4 plus; blood pressure, 210 over 110; pulse, 112; œdematous; nitrogen retention; eye ground vessels tortuous and dilated. Dial-urethane 4 cubic centimeters was administered and a Vorhees bag inserted and inflated. Four hours later, the bag was expelled and immediately after a live fetus was born. There was no bleeding and complete recovery followed.

CASE 5. Primipara, aged 28 years; 6 months pregnant. Patient was profoundly toxic, had a small vagina and long tight cervix. She was given dial-urethane 4 cubic centimeters, plus morphine $^1/_{24}$ grain. The cervix was dilated and a Vorhees bag was inserted and inflated. In toxic cases in which fetal life is not to be considered, great help can be had by adding morphine $^1/_{24}$ to $^1/_{12}$ grain. The uterus was left to empty itself which it did 24 hours later.

Interesting data as to the permissible dose of dial-urethane are contained in the papers of Muller and Hoven. These authors employed the preparation for "narco-sustained" therapy in patients with mental disturbances; bringing about unconsciousness for prolonged periods during a period as long as 10 days. By either intravenous or intramuscular injection, they believe that the single dose should not exceed 4 cubic centimeters nor should the amount given in 24 hours be

greater than 8 cubic centimeters. One should recognize, however, that scopolamine or opium preparations were administered simultaneously and that the treatment was carried out over a period of days. Muller is of the opinion that renal insufficiency and respiratory tract infection are contra-indications to the use of dial-urethane solution in the massive dosage necessary. Irving and his associates likewise hold the belief that barbiturates should not be used in obstetrics "when the patient has any infection of the upper or lower respiratory tract." To this, I cannot subscribe; dial-urethane, in the dosage employed by me, has seemed especially serviceable during a recent epidemic of influenza, where I resorted unhesitatingly to its injection in 6 patients with more or less severe infection, and encountered no evidence of untoward results. In these patients I am convinced that ether, certainly, would have been most dangerous, and I am by no means sure that even nitrous oxide-oxygen could have been given with impunity. It is worthy of note that Muller finds the dangerous period under dial-urethane from the third to the fifth day of administration; much later than the effect would persist in any parturient patient. With dial-urethane analgesia carried out as described, it is possible to rouse the patients at any time sufficiently to have them take liquids, and this is always done in cases of prolonged labor.

Hussy felt that dial stimulated uterine contractions; McNeile and Vruwink state that the dial-urethane solution hastens cervical relaxation; Nelson is of the opinion that labor is materially shortened by the preparation. My experience, also, leads me to conclude that dial-urethane, in most cases, is responsible for more prompt delivery; although in rare instances, it may cause some delay. It is not clear how this result is accomplished. Certainly, cervical relaxation seems favored; furthermore, I have the impression that uterine contractions are increased in force and frequency, but definite proof of this is lacking. In no instance have I observed undue tendency to postpartum bleeding, but it should be mentioned that my routine practice is to inject 1 cubic centimeter of pituitary solution at the conclusion of the third stage.

As to the possibility of carrying out operative procedures under dial-urethane analgesia, my experience does not coincide fully with that of Nelson, who, apparently, never found recourse to supplementary anæsthesia necessary for "forceps, versions and extractions, episiotomies, and necessary repair." In all our cases requiring episiotomy or perineal repair, provision is made for administering ether by inhalation. A few cases require a small amount of ether; others do not.

Restlessness, so frequently a troublesome feature after amytal and apparently after pernocton and pentobarbital (6), has been practically absent in my series under dial-urethane. We have had one patient who had to be restrained. A few others were slightly restless but not sufficiently so as to be particularly annoying. However, the importance of having the patient constantly under the observation of a responsible attendant until consciousness is fully recovered cannot be too strongly stressed.

There is usually a slight fall in blood pressure immediately after the injection, but this has never been alarming and the pressure soon returns to normal. Marney warns against too rapid injection, stating that respiratory depression may result unless this precaution is observed. With the rate I have recommended (not over 1 cubic centimeter per minute), no disturbances of this nature have been noted. Double vision, as reported by Nelson, is not infrequent but soon passes off. Cutaneous rashes have not occurred in any of my patients but may result from administration of dial.

It is gratifying to state that in my cases there have been no stillbirths, nor have I encountered any instances of serious respiratory depression in the child. This is a pleasing contrast to what is seen after administration of adequate doses of morphine or other opium derivatives and differs also from the experience of Irving and his associates after employment of amytal, pernocton, or pentobarbital.

At any time if the patient is slow to recover or seems depressed, the condition may be corrected by intravenous injection of coramine, marketed in ampuls and stated to be a specific

in all cases of barbiturate depression. The dose varies, but as much as 10 cubic centimeters can be used at a single injection, as pointed out by Hoven. We have not found it necessary for a mother, but we always have the ampuls on the table for injection into the umbilical vein in case the infant manifests respiratory depression.

SUMMARY

The dial-urethane solution in ampuls seems to be a safe and effective obstetrical analgesic.

"Biological" dosage is recommended; that is, the slow intravenous injection of the solution (not over 1 cubic centimeter per minute) until the patient no longer responds to questions. Subsequent injections of 2 cubic centimeters may be employed as necessary; but the initial dose should not exceed 4 cubic centimeters nor should the total during 24 hours be in excess of 8 cubic centimeters except in unusually large patients.

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CLINICAL SURGERY

FROM THE LAHEY CLINIC

INTRATHORACIC GOITER

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ANATOMICAL CONSIDERATIONS

IN order to understand the mechanism whereby a tumor arising in the thyroid gland, which is entirely extrathoracic, may eventually become entirely intrathoracic, it is essential that the anatomy of the thyroid gland be visualized. Because of the location of the gland, it is involved in the motion of swallowing, it bears relation to the pretracheal and prevertebral fascia, and it is placed in a plane which leads into the superior mediastinum; the covering of the gland with prethyroid muscle has a tendency to guide tumors of the thyroid gland into the superior mediastinum. We know, in addition, that in its development the thyroid descends from its origin in the fetus at the base of the tongue, occasionally progressing even beyond the normal into the mediastinum. This last factor we have found to have little to do with intrathoracic goiters; in an experience now amounting to over twelve thousand operations, we have never seen an intrathoracic goiter which we felt was the result of an excessive developmental descent of the thyroid gland.

The thyroid gland is located on the upper tracheal rings. In front of it are the prethyroid muscles attached to the sternum and the sternoclavicular junction and behind it is the prevertebral fascia. The glands ascend and descend with each act of swallowing in this muscular and fascial plane which leads, as stated, directly into the mediastinum.

Therefore, when an adenoma of either lobe or the isthmus of the thyroid enlarges it must make room for itself in one of two directions: it either causes the prethyroid muscles to bulge forward thus producing a projection of the neck, in which case it is obviously an extrathoracic goiter or it projects downward into the mediastinum, in which case it is an intrathoracic goiter.

A lateral silhouette of the upper part of the thorax shows that the thorax tends to taper toward the neck, spreading out as the chest widens downward toward the diaphragm (Fig. 1).

When an adenoma has passed the upper thoracic aperture, as indicated by the arrow in Figure 1, and has become intrathoracic, as we have repeatedly stated in discussing this subject, it can increase its diameter only by descending and it is this widening of the more or less spherical adenoma or cyst which, due to the tapering of the chest, pushes it lower and lower into the mediastinum.

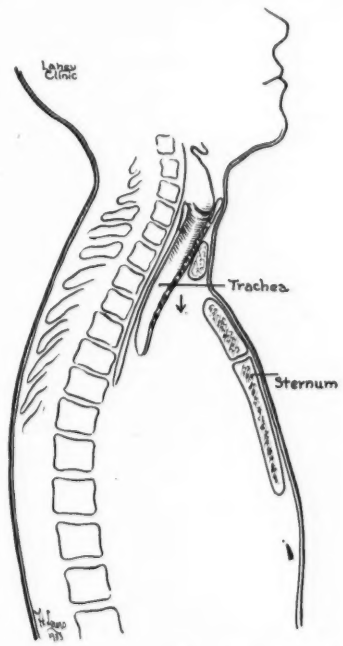

Fig. 1. Note the taper of the chest as seen in lateral silhouette, showing how increase in diameter of a spherical adenoma as shown in Figure 6 causes it to descend further into the mediastinum.

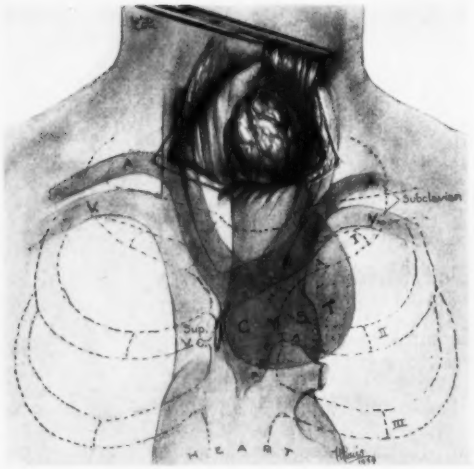

Fig. 2. A diagrammatic illustration of an intrathoracic cyst (degenerated adenoma) which produced the nearest escape from a fatality on the operating table from choking seen in our experience—cyanosis, unconsciousness, and complete absence of air entering lungs. Emergency puncture of the cyst resulted in immediate and complete relief of obstruction permitting deliberate removal of the sac.

Fig. 3a. Note the anteroposterior pressure on the trachea by an intrathoracic adenoma most marked at the point indicated by the arrow. The anterior line of the trachea displaced backward has been made more definite by small ink dots.

Occasionally the statement is made that patients with exophthalmic goiter (primary hyperthyroidism) have intrathoracic goiters. Never, in our experience, have we seen exophthalmic goiter or primary hyperthyroidism—hyperthyroidism with true hyperplasia—become truly intrathoracic. In men, the lateral lobes are lower than in women but never truly intrathoracic in our experience.

The most common type of intrathoracic goiter is the discrete adenoma; in the region where goiter is endemic, the nodular multiple adenomatous goiter of the endemic type is, of course, the most common. Occasionally cysts which are entirely intrathoracic are seen; in fact, the nearest escape from a fatality by immediate choking which I have ever seen was in a patient with intrathoracic goiter who had a large intrathoracic thyroid cyst (see Fig. 2). These cysts, however, originally were thyroid adenomata but the adenomatous element within the capsule became necrotic, was absorbed, and replaced by fluid. Therefore, the fact that intrathoracic thyroid cysts do occur is further evidence that in practically all of the cases the cysts are adenomatous in origin.

Occasionally a diffuse colloid goiter is partly intrathoracic, but almost never does such a goiter become frankly intrathoracic. The explanation for this is that the diffuse colloid goiter is usually the result of an early degenerative change in the gland preceding the appearance of the multiple nodules which are scattered throughout the gland and which are so characteristic of endemic goiter. The diffuse colloid condition as a rule indicates a progressive state. The degenerative process rarely remains stationary; if the goiter has existed long enough to become intrathoracic, and descent into the thorax takes time, the transition has usually taken place from a diffuse colloid goiter into a goiter of the multiple nodular endemic adenomatous type. Therefore, for practical purposes, all intrathoracic goiters should be considered as adenomatous in type—the discrete adenomata, the multiple adenomata, or the thyroid cysts which were originally adenomata.

CLINICAL SIGNS OF INTRATHORACIC GOITER

The clinical signs of intrathoracic goiter are produced almost entirely by pressure upon the trachea and the internal jugular veins. Rarely is there injury to the recurrent laryngeal nerve as a result of the intrathoracic extension of an adenomatous goiter (see statistical figures later in paper).

The reason that the recurrent laryngeal nerve does not become paralyzed even in the presence of an enormous intrathoracic goiter is un-

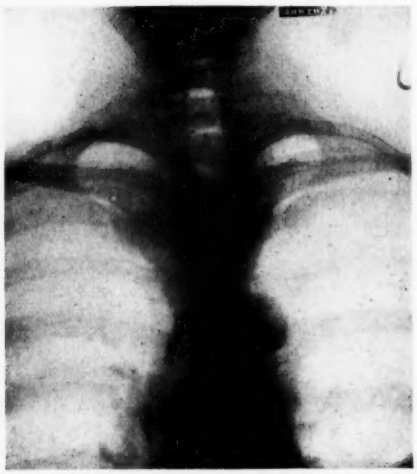

Fig. 3b. Note the wide trachea in the same case made more clear by ink dots. The widening is the result of anteroposterior pressure.

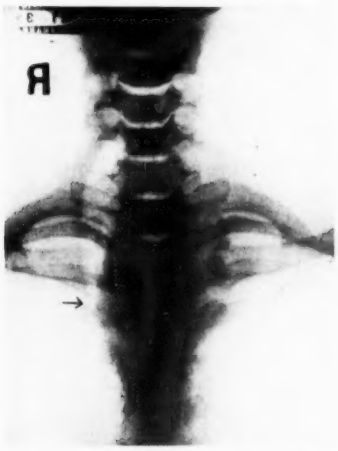

Fig. 4. Lateral deviation and narrowing of the trachea at the point indicated by arrow, due to an intrathoracic adenoma of the thyroid located lateral to the trachea. This is the most common type of intrathoracic goiter.

doubtedly the fact that the growth of the intrathoracic tumor is very gradual, thus causing slow stretching of the recurrent laryngeal nerve. As the stretching is so slow and so gradual the nerve is thus able to elongate its fibers and to adjust itself to its distorted position without interruption of its conductivity. In our experience recurrent laryngeal paralysis in intrathoracic goiter is so rare that when it does occur, we are extremely suspicious that it is the result of malignant degeneration of the adenoma and furthermore we suspect that the recurrent nerve is involved in the malignancy.

In intrathoracic goiter three types of tracheal pressure effects are noted:

1. Anteroposterior pressure, when an adenoma arises in the isthmus of the thyroid, descends behind the sternum in the middle line, and collapses the trachea from before backward, as shown in Figure 3, a and b.

2. Lateral pressure is the most common and occurs as the result of lateral deviation of the trachea—as shown in Figures 4; 5a, b, c, and d; 6a and insert, b, and c; 7a and b; 8; and 9. Adenoma of the thyroid usually arises in one of the lateral lobes of the gland and, even though an adenoma does not arise entirely within a lateral lobe, as it enlarges, it tends to topple to one side or the other of the trachea which stands out as a semi-rigid tube.

3. Bilateral pressure. The next most common type of tracheal pressure is bilateral pressure, as illustrated in Figures 10a and b, and 11. Bilateral pressure is caused by a bilateral complete or incomplete intrathoracic goiter which collapses the trachea by pressure on either side. Sometimes the pressure is so great that the lumen of the trachea is merely a slit.

Clinically pressure on the trachea, as the result of complete or incomplete intrathoracic goiter, produces varying degrees of respiratory difficulty. It must be borne in mind that the narrowing of the trachea in these cases progresses so slowly and gradually that patients readily become adjusted to a diminished space for air intake and also to the associated stridor. These patients, as was true in the patient whose roentgenogram is shown in Figure 10a, become so used to hearing their own noisy breathing that they frequently fail to be impressed by it until attention is called to it by strangers.

When tracheal obstruction occurs within the thorax, particularly as shown in Figure 6a, there will occasionally be peculiar attacks of suffocation at night when the patient is asleep. Patients with intrathoracic goiter and tracheal narrowing state that they are occasionally awakened in the night by choking, that they struggle violently, then regain their breath after a real ordeal, and go back to sleep. Witnesses to these attacks have stated that patients become extremely cyanotic and that the danger of sudden death from suffocation at times seems imminent in the struggle for breath.

Fig. 5a

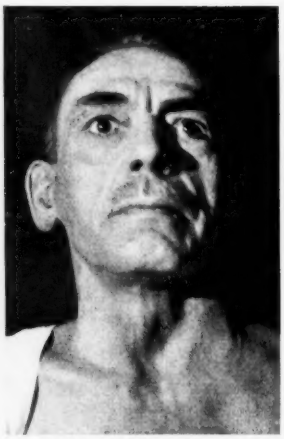

Fig. 5b

Fig. 5d

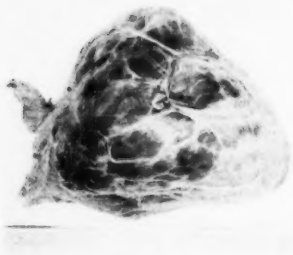

Fig. 5c

Fig. 5a. A roentgenogram of a moderately large intrathoracic goiter showing moderate deviation of the trachea and descent to a little below the level of the arch of the aorta.

Fig. 5b. A photograph of the same patient showing absence of goiter on neck. One can also faintly see the dilated superficial thoracic veins near the sternal notch.

Fig. 5c. A photograph of a cross section of the intrathoracic adenomatous mass demonstrating its dimensions.

Fig. 5d. A roentgenogram of the mediastinum 3 weeks after removal of the intrathoracic mass showing the return of the trachea to the midline and the return of its caliber to normal.

The explanation of this phenomenon, we believe, is that a plug of tenacious mucus accumulates in the bronchus at night while the patient sleeps, lodges in the narrowed trachea, as seen at the intrathoracic level of the trachea indicated by the arrow in Figure 6a, produces obstruction, and becomes stuck there, finally to be dislodged by the violent efforts of the patient in his struggle to get air into his lungs. When such a history is presented by a patient, the presence of an intrathoracic goiter should be suspected and the patient subjected to an X-ray examination of the superior mediastinum to demonstrate the position and caliber of the trachea.

Another complaint associated with intrathoracic goiter, particularly when the adenoma is located laterally in the chest, as shown in Figure 6a and insert, is that the patient is able, for example, to sleep with the right side of his head on the pillow but cannot sleep with the left side of his head on the pillow, or vice versa. This is due to the fact that the trachea is collapsed laterally and when the head is angulated, as shown in Figure 6a insert, the trachea closes even more closely and thus obstruction to respiration is produced, causing the patient to choke, wake up, and change his position.

Complete or incomplete intrathoracic goiter of any extent is rarely seen without dilatation of the superficial thoracic veins, Figures 12a, b, c, and d. The dilatation varies with the amount of pressure exerted by the goiter on the internal jugular system and the amount of interference with the return blood supply from the head; compensatory dilatation of the superficial thoracic venous system is established to take up the work of the obstructed internal jugulars. Therefore, the presence of a mediastinal lesion should always be suspected in the presence of dilated, superficial thoracic veins.

Another clinical feature occasionally seen should make one suspicious of intrathoracic

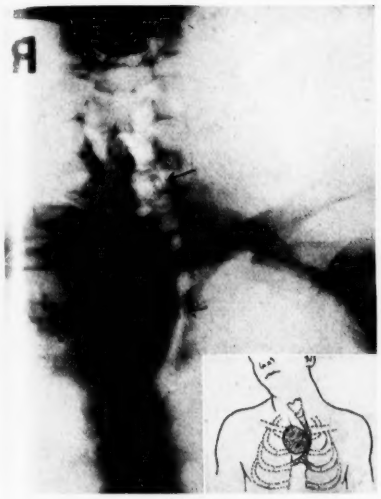

Fig. 6a

Fig. 6b

Fig. 6c

Fig. 6a. Showing the typical spherical intrathoracic adenoma of the thyroid with marked deviation of the trachea and narrowing from lateral intrathoracic pressure. Note the normal caliber of the trachea at the level of the upper arrow and the narrowing at the intrathoracic level of the arrow at which narrow point a plug of inspissated mucus may lodge at night and produce choking and the condition described in the text. The insert shows the type of discrete intrathoracic adenoma which also occasionally makes it impossible for a patient to sleep with the head on one side as illustrated in diagrammatic illustration and described in the text.

Fig. 6b. A photograph of the patient, which demonstrates the complete absence of any visible goiter on the neck.

Fig. 6c. Compare with Figure 6a. This was taken 3 weeks after operation. Note the gradual return of the trachea toward the midline together with gradual increase in the caliber of the trachea following the removal of pressure from it.

goiter and that is the thickening of the skin over the face, due to œdema resulting from interference with the return of venous supply from the head (Fig. 13). We have seen a few patients who have had a definite puffiness of the face which was immediately relieved on the removal of the intrathoracic masses.

When the intrathoracic goiter collapses the trachea from before backward, as shown in Figure 3, the patient not infrequently complains of an inability to bend over. Bending over produces greater pressure upon the trachea, shuts it off, and the patient chokes. He has learned, for example, that it is not possible for him to bend over and tie his shoes without choking. The finding of this symptom should make one suspicious of the presence of intrathoracic goiter.

Figure 14 illustrates the unusual combination of intrathoracic goiter and a pulsion œsophageal diverticulum in a patient who 15 years previously had had removed an intrathoracic goiter on the same side as the diverticulum. We first remove the diverticulum and will later remove the remaining partly intrathoracic goiter on the left. To remove the intrathoracic goiter on the left first, might well complicate the removal of the diverticulum.

In Figures 14, 15, 16, 17, and 18, one may observe the depths well below the arch of the aorta to which the very deep intrathoracic goiters may descend.

We have been interested in reviewing our experiences with intrathoracic goiter for the purpose of confirming or dispelling certain impressions forced upon us by our somewhat large series of cases.

From the year 1915 to July 1, 1933, there were 4,363 cases of exophthalmic goiter or primary hyperthyroidism in which operation was carried out in the clinic. During this time there were 5,131 cases of adenomatous goiter in which operation was done in the clinic. This latter group includes adenoma as well as adenomatous goiter.

Of this group of 5,131 adenomatous goiters, 1,086, or 21 per cent, extended downward from the usual position of the thyroid gland into the superior mediastinum and thorax.

We have divided all goiters extending downward into two grades: the first, those in which the mediastinal extension is nearly to the arch of the

Fig. 7a. Marked pre-operative deviation of the trachea in a case of partly intrathoracic goiter as indicated by dashes and arrows. Note that there is no marked narrowing of the trachea due to the fact that most of the goiter is extrathoracic.

Fig. 7b. An X-ray to show the return of the trachea to its normal position after removal of the adenoma, the lateral pressure of which caused its marked deviation.

aorta; the second, those which extend to the arch of the aorta or beyond this level.

Of the 1,086, 745, or 68 per cent, were of the first variety, while 341, or 32 per cent, were of the second variety.

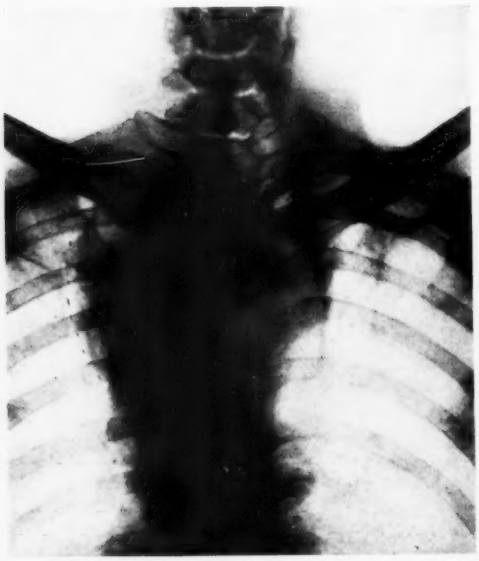

Fig. 8. A typical very large and very deep unilateral intrathoracic goiter with tracheal deviation and extending well below the arch of the aorta. Note the marked deviation of the trachea outlined by ink dashes and indicated by arrow.

Fig. 9. A typical deep intrathoracic goiter extending to and beyond the level of the aortic arch. The characteristic lateral deviation of the trachea may be noticed in this instance also. The aortic arch is indicated by the arrow.

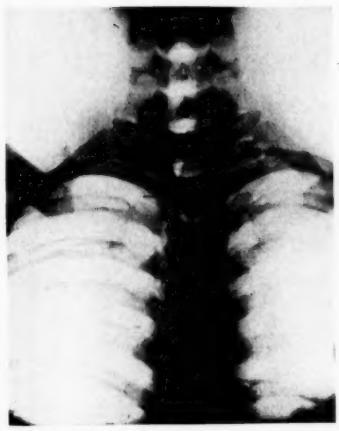

Fig. 10a. Bilateral pressure on the trachea by a bilateral intrathoracic adenomatous goiter. Note the normal width and caliber of the trachea at level of the upper arrow and the bilateral collapse of the trachea to a narrow line at the level of the lower arrow where the bilateral adenomata are intrathoracic. In this picture one can visualize how intrathoracic goiters cause narrowing of the trachea. The adenomata in the mediastinum rest externally against the rigid chest wall and as they enlarge must collapse the compressible trachea which is interposed between the two enlarging adenomatous lobes.

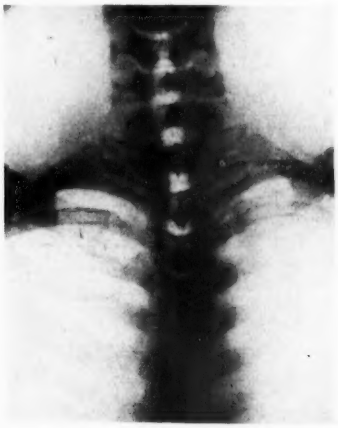

Fig. 10b. Compare the pre-operative picture, Figure 10a, with Figure 10b, the postoperative picture, taken after removal of the intrathoracic adenomata. Note that with the removal of the pressure on the trachea it has almost entirely regained its normal caliber.

As stated there was not a single instance in which the hyperplastic gland of an exophthalmic goiter became truly intrathoracic.

The upper pole of the thyroid gland occasionally extends behind the larynx or trachea at its normal level in such a manner as to produce obstructive symptoms by pressure on the back wall of the larynx which is unprotected by the thyroid cartilage. Such a condition occurred in 46 cases in our series. Also, the gland of the patient with exophthalmic goiter may rarely extend behind the pharynx; we have 4 such cases in our series.

The age had little to do with the predominance of one of either group of intrathoracic goiters over the other.

Based upon 100 unselected cases, the average age in the first group was 52 years; in the second, 48 years. The average age for the whole group was 50 years indicating as already stated that it takes time for a goiter to progress downward from its normal position into the mediastinum and so the condition commonly occurs in middle and late life and rarely in young people.

The sex incidence corresponds quite consistently to the relation of goiter to sex and has as would be expected, little or no relation to this condition.

	Males	Per cent	Females	Per cent
Of Group I descent.....	68	9	677	91
Of Group II descent....	64	18	277	81

The incidence of laryngeal paralysis due solely to the goiter and not to the operation, as already stated, was small: in Grade I, 3 of 745 cases; in Grade II, 4 of 341 cases.

Fig. 11. The marked degree of narrowing at the level indicated by arrow which can occur with bilateral pressure from bilateral intrathoracic goiter.

Fig. 12, a and b. Dilatation of the superficial venous system in large intrathoracic and extrathoracic goiters.

Fig. 12, c and d. Marked dilatation, particularly in the region of the sternal notch of the superficial veins in large completely intrathoracic goiters.

The effect on the trachea by pressure or deviation as shown by X-ray was: In Grade I, deviation in 93 per cent, no deviation in 7 per cent; in Grade II, deviation in 98 per cent, no deviation in 2 per cent.

As one learns from dealing with these cases in numbers, and as may be seen in the X-ray illustrations, intrathoracic goiter will rarely be present without some degree of tracheal pressure as evidenced by lateral deviation, anteroposterior narrowing or bilateral collapse.

The incidence of obstructive symptoms was more marked as would be expected, in the Grade II descents.

INCIDENCE OF OBSTRUCTIVE SYMPTOMS

	None Per cent	Mild Per cent	Severe Per cent	Unknown cases
Grade I	53.2	40	6.8	12
Grade II	35	41.5	23.5	9

To prove that the development of intrathoracic goiter could be avoided by frequent examinations and the removal of those goiters which tend to descend into the thorax and to prove that it takes time for a goiter to become intrathoracic, the duration of the goiter was ascertained in 100 cases in each group. In Grade I, the duration of the goiter was 13.04 years; in Grade II, 15.10 years.

The fact that obstructive symptoms late in the presence of the goiter brought many of these patients to the clinic for operation is verified in the histories of 100 unselected cases which show that although these patients had had goiters for an average of 14 years, they had had obstructive symptoms for an average of only 1½ years before coming to us for operation.

Since most goiters which have become intrathoracic are adenomatous in character, it is not surprising that in both Grade I and Grade II 70 per cent of the cases were non-toxic and 30 per cent showed thyroid toxicity.

As intrathoracic extension of thyroid tissue into the mediastinum theoretically brings about considerable anatomical distortion, one would suspect that there might be a high percentage of operative injury to the recurrent laryngeal nerve and to the parathyroid glands. Likewise, as the

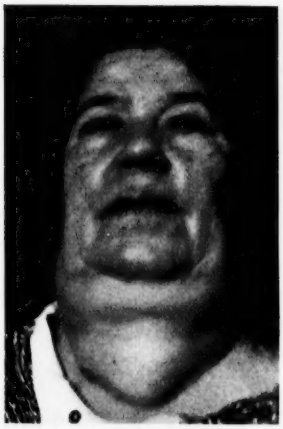

Fig. 13.

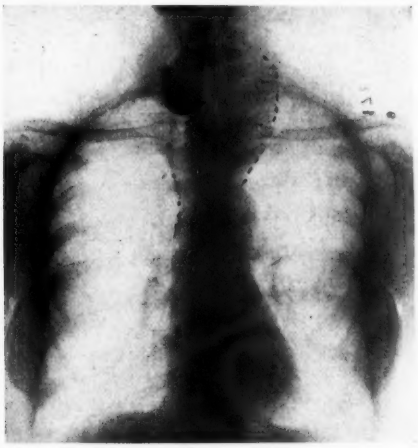

Fig. 14.

Fig. 15.

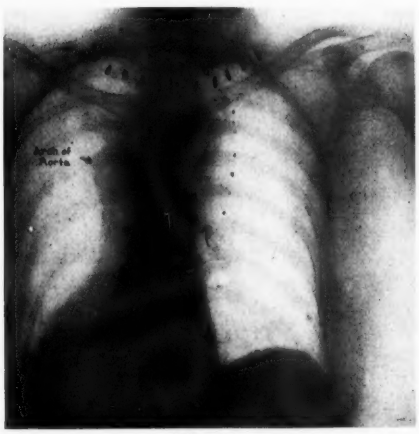

Fig. 16.

Fig. 13. The thickening of the skin over the face due to œdema, the result of an enormous intrathoracic goiter, causing pressure at the superior thoracic strait on both internal jugular veins.

Fig. 14. An unusual combination of pulsion œsophageal diverticulum on right and intrathoracic goiter on left. This patient had had an intrathoracic goiter removed from the right side 15 years previously. Note the deviation of the trachea, marked with dots, on the right and outline of the intrathoracic goiter on left, and the œsophageal pulsion diverticulum on the right.

Fig. 15. A deep intrathoracic goiter well below the level of the arch of the aorta.

Fig. 16. The depth to which an intrathoracic goiter can descend. As may be seen from the clips on the goiter incision, this is an immediately postoperative X-ray of the mediastinum and the cavity remaining after removal of a deep intrathoracic goiter has been packed with gauze. Note on the left the level of the arch of the aorta and on the right, outlined by dots, the shadow of the gauze filled pocket in the mediastinum. Note the lowest level, indicated by a second arrow, well below the level of the aortic arch.

mediastinum is widely opened and drained in this operation and as it is at times a technically difficult procedure to remove deep intrathoracic goiters, one might suspect that there would be a high mortality in this group of cases and in addition a high incidence of tracheotomy. In order that we might visualize our statistics as relates to fatalities and the complications mentioned, we have tabulated our figures as shown in Table I.

Fig. 17. A postoperative X-ray picture after removal of a very deep intrathoracic goiter with roentgenographic ureteral catheters introduced into the resulting cavity to demonstrate its depth. Note at the level of the arrow the lowest roentgenographic catheter and its relation to the arch of the aorta.

It is of interest to note the definitely higher mortality rate in the deeply located Grade II intrathoracic goiters as compared with Grade I, less deeply located goiters. This added mortality rate in these deep goiters is an additional argument in favor of the removal of goiters which are tending to become intrathoracic before they do become intrathoracic.

INDICATIONS FOR SURGERY

If we would establish the principle of examining all patients with goiters frequently, we will say perhaps once a year, and removing the growth before it becomes intrathoracic, much of our difficulty in treating this condition could be prevented.

Once a goiter has become definitely intrathoracic, it should be removed, for if it is allowed to remain it will doubtless increase in size and, as this enlarges, it tends more and more to produce symptoms, it becomes more and more difficult to remove, the mediastinum must of necessity be more and more widely opened, the patients have become older and the risk of operation therefore

Fig. 18. An enormous intrathoracic multiple adenomatous goiter. Due to the calcification of the capsules of the adenomata, the extreme depth of this intrathoracic goiter can be visualized.

greater. We, therefore, repeat that all goiters which are tending to become intrathoracic and all which have become intrathoracic, should be removed.

Since we have published elsewhere our technique for the removal of intrathoracic goiter[1] we do not wish to repeat it in this discussion. Because of the importance, however, of the type of anæsthesia employed in these cases and because the matter of anæsthesia plays a considerable part we feel sure in the mortality, particularly in the very deep intrathoracic goiters, we do want to discuss this part of the operative management of this condition.

ANÆSTHESIA

The best anæsthesia for intrathoracic goiter, in fact, the only anæsthesia with which it is safe to remove any large intrathoracic goiter, is intratracheal anæsthesia. Whether one employs ether, nitrous oxide gas, ethylene, or cyclopropane, the most recent anæsthesia which we are now employing experimentally, it then becomes purely a matter of the anæsthetist's choice so long as an intratracheal catheter has been introduced.

In all intrathoracic goiters in which there is any considerable narrowing of the trachea and in which the intrathoracic tumor is of any considerable size, there will always be the danger of difficulty in making the tumor pass through the

[1]The surgical management of intrathoracic goiter. Surg., Gynec. & Obst., 1931, liii, 346–354.

TABLE I.—IMMEDIATE POSTOPERATIVE COMPLICATIONS

IN GRADE I INTRATHORACIC GOITER

Year	Tetany	Postoperative laryngeal paralysis unilateral	Tracheotomy	Death	Mortality per cent
15–1925 95 cases	0	1	1	4	2.4 /10
25–1930 32 cases	0	2	2	1	.3 /10
30–1933	1	5	0	1	1.4 /10

IN GRADE II GOITER

15–1925 94 cases	0	4	0	6	9.3 /10
25–1930 76 cases	0	4	3	5	4.3 /10
30–1933 91 cases	0	5	2	4	2.5 /10

The causes of death in the 21 fatalities were as follows:

	Cases
Pneumonia	3
Cerebral hæmorrhage	1
Thyroid crisis	5
Diabetes	2
Embolism	1
Postoperative hæmorrhage and shock	3
Œsophageal fistula	1
Mediastinitis	2
*Bilateral laryngeal paralysis	1
Early cases with cause unknown	2

*Dissection of both recurrent laryngeal nerves at autopsy in this case showed them to be intact and uncut. This patient had tongues of thyroid tissue completely encircling her trachea and her bilateral paralysis was doubtless due to stretching of the recurrent nerves in the removal of these tongues of thyroid tissue.

upper thoracic strait, thus producing pressure upon the trachea and without an intratracheal catheter causing the danger of suffocation.

It should be borne in mind in dealing with tracheal obstruction in intrathoracic goiter that the performance of tracheotomy is extremely undesirable: (1) because the obstruction to the trachea in intrathoracic goiter, being within the thorax, is usually too low to be dealt with satisfactorily by means of the ordinary short tracheotomy tube, and (2) because the mediastinum has been widely opened and a tracheotomy in the presence of an open mediastinum seriously presents the possibility of infection in this region and mediastinitis.

We, therefore, feel that except in those goiters which are only partly intrathoracic and which obviously can be readily delivered, whatever type of anæsthetic is employed, it should be administered through a previously introduced intratracheal catheter. With the tube in place, any amount of manipulation and pulling, hauling, and prying of the mass out of the mediastinum can be undertaken without danger of interfering with the respiration.

CONCLUSIONS

Any patient with mechanical interference to breathing should be suspected of having an intrathoracic goiter and should be subjected to an X-ray examination of the mediastinum.

In the presence of an intrathoracic goiter, deviation or flattening of the trachea either laterally or anteroposteriorly together with the mediastinal shadow can be demonstrated in practically all cases.

Dilatation of the superficial thoracic veins should always make one suspicious of the presence of an intrathoracic goiter.

Any goiter which is low-lying and tends to become intrathoracic should be removed before it becomes intrathoracic.

The introduction of a catheter between the vocal cords into the trachea makes the removal of large and difficult intrathoracic goiters infinitely more safe.

Statistics are given showing the incidence of Grade I and Grade II intrathoracic goiters. Figures are also submitted showing the age incidence, sex incidence, the incidence of preoperative and postoperative laryngeal paralysis, the incidence of tracheal deviation or pressure, the incidence of obstructive symptoms, the duration of the goiter, the incidence of hyperthyroidism, the immediate postoperative complications and the mortality rate together with the cause of death in 21 cases in a group of 1,086 patients operated upon with partly or completely intrathoracic goiters.

FROM THE STYRSÖ COAST HOSPITAL, GOTHENBURG

INTERPOSITION OF OS PURUM IN OSTEOSYNTHESIS AFTER OSTEOTOMY, RESECTIONS OF BONES AND JOINTS, (INTERPOSITION-OSTEOSYNTHESIS)

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IN a recent article[1] entitled "Osteoplastic Cuneiform Osteotomy in the Treatment of Ankylosis," I explained how fairly large sized pieces of boiled autoplastic bone heal in when transplanted in connection with an osteotomy affecting the diaphysis or the epiphysis. The characteristic features of the healing in process, which was observed by means of a series of roentgenograms taken at intervals and as long as 465 days after the operation, were: (1) that the boiled bone grafts healed in primarily; (2) that they appeared to be able, without collapsing, to support the mechanical strain to which they were subjected; and (3) that the regeneration of bone in the epiphyseal transplants was endosteal, i.e., regeneration took place within the graft, whereas in the diaphyseal transplantations regeneration of bone was mainly periosteal in that the newly formed bone developed to a great extent beneath the periosteum outside the graft. I also pointed out that as centrally located, minor necroses remain for some time in the higher and bulkier parts of wedge shaped grafts, it should be advantageous to use graft material free from connective tissue, albuminous substances and fat, os purum, so that the canal system of the bone would thus be more easily accessible to the living cells which grow into the canals from the surrounding tissue. I stated, too, that I was engaged in making surgical tests of such bone material.

The graft material I use is both homoplastic, obtained from amputations, and heteroplastic, obtained from the slaughter houses. In either case the material is immediately freed of soft parts and is then subjected to a very lengthy chemico-physical process of purification, the fat, albuminous substances, and connective tissue being dissolved and extracted, so that the canal systems in the lime residue remain open. We have kept this graft material in a dry condition in sterile glass vessels for longer or shorter periods of time before using; immediately before use the material needed is boiled for about 10 minutes in a physiological salt solution. Such graft material is easy to manipulate for surgical purposes; it is porous and its open, clean canal system makes easy the absorption of blood and tissue serum when the graft is implanted in the tissues.

In this paper I shall describe the technique and instruments used in these bone transplantations, and will show roentgenograms of some cases in which I have employed these grafts. In my contribution entitled "Studien ueber Knochenimplantation und Knochenneubildung, Implantation von 'os purum' sowie Transplantation von 'os novum,'" I have described the process in detail.

In an epiphyseal cuneiform osteotomy, it has been found very easy (1) to secure fixation of the bone wedge because of the friction of the spongy surfaces and (2) by means of the graft, to retain the ends of the bones in good position in relation to each other. In a diaphyseal osteotomy, however, it was—as I have also found in subsequent similar operations—difficult to keep the graft in position because of the hard, smooth surfaces of the bone, the ends of which easily slipped in relation to each other.

I have for this reason, especially as it affects the diaphyseal operations, elaborated the operative technique and shaped the graft so that when it is feared the bones may slip in relation to each other, the graft by its very form will remain in place between the ends of the bones and fix the bones in relation to each other, without thereby adversely affecting the action of the bone generating tissues. For instance, if the graft is shaped like a sphere, is of suitable and proper size, and is inserted exactly between the ends of the bone after an osteotomy or after a transverse fracture of the long bone, it will partly penetrate into the medullary canals of the respective ends of the bone and will be kept in position by the action of the surrounding, contracting musculature. By this means the ends of the bone will also be kept in the desired position in relation to each other. Such an interior fixation becomes effective if the movements between the ends of the bone are furthermore fixed in the usual way by means of externally applied surgical or orthopedic fixation devices.

J. Bone & Joint Surg., 1932, xiv, 643–654.

The insertion of the graft between the ends of the bone after an osteotomy, the resection of bones, or the like, may cause trouble and difficulty. It is difficult with the customary surgical instruments to distract in a longitudinal direction the ends of the bone of the extremities. If, however, one makes use of a distractor which I have designed for the purpose, the procedure will very likely not entail any great difficulty. At one end this instrument is shaped like a chisel, the other end is provided with a transverse handle (Fig. 1). The edges of the chisel end are faceted like a prism; they are meant to give support and, when pressure is applied, to grip the ends of the bone without slipping on them. To produce distraction, the chisel end of the distractor is inserted between the bone fragments of the osteotomy, fracture, etc. (Fig. 2 a). When a suitable position in relation to the bone fragments is reached, the instrument is rotated upward by a quarter turn around its longitudinal axis; thus the ends of the bone are separated from each other the breadth of the chisel end (Fig. 2 b). Thereupon the graft, which has been suitably shaped before the operation as determined by the roentgenograms, is inserted between the ends of the bone by means of a pair of fenestrated angular tongs, or the like, after which the chisel is rotated back and is withdrawn. The muscular tonus now forces the ends of the bone together, so that the graft is partially surrounded by the medullary canals, thus locking the ends of the bone together.

However, should the width of the chisel of the distractor be insufficient to achieve the necessary space between the ends of the bone, another distractor, with a broader chisel end, must be taken and inserted beside the previous one and rotated, so that a greater distance between the ends of the bone may be obtained. With a series of distractors with chisel ends of different breadths (Fig. 1), the operator will be prepared for such eventualities. This method is best suited for operations upon the epiphyses. Care should be used when rotating the distractor to protect the spongy part by means of thin bone or steel spatulas (Fig. 6), which serve as protection between the instrument and the bone, and also as gliding surfaces for the roughened spongy graft. Manipulation of the extremities is also of assistance in inserting and adjusting the graft. Finally, if it is found necessary, a lever, a "guide lever" designed by me, can be used. By means of this lever one of the bone fragments together with the graft fitted into the medullary canal, in the course of levering up, is pushed and guided against the other fragment (Fig. 3). This last mentioned

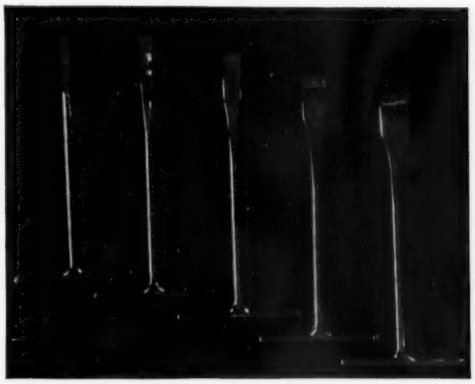


Fig. 1. Series of distractors with various breadths of chisels.

method is often found suitable in diaphyseal operations.

If, now, a spherical graft has been adjusted between the ends of the bone in such a way that it projects for some distance into the medullary canals on either side, the ends of the bone can afterward not be dislocated laterally, but easily toward the periphery and axis if the sphere is sufficiently large. Dislocation longitudinally is prevented, after the adjustment of the graft, by muscular tension. Such an osteosynthesis will, therefore, form, and the bone fragments during the ensuing fixation treatment can be conveniently adjusted in relation to each other.

In osteosynthetic treatment of fractures, the method here described might be used when dealing with transverse fractures of long bones, and in the case of other minor oblique fractures. In very oblique, or in spiral, fractures, or in fractures in the epiphyses, the synthesis must be carried out in some other way, preferably by the use of ordinary bone pegs, tongue shaped or lamellar pieces of bone, in combination with uniting sutures. The bone peg, and tongue shaped or lamellar pieces of bone are driven into holes, drilled into the compact mass in several places, or into grooves cut with a circular saw, or direct into the spongy mass, so that a dislocation lateralward and toward the periphery is prevented.

The bone pegs should be shorter than the breadth of the chisel end of the distractors, so as to enable the pegs to be easily interposed by means of the distractor.

I have carried out osteotomies by drilling holes through the bone in one and the same plane, and then breaking the bone through in this plane by means of a chisel. For boring these holes I have

Fig. 2. a, left. The distractor is inserted between the ends of the bones. b, The distractor after rotation.

employed the very perfect drilling machines used by dentists. The shanks of the drills in these machines are extremely light and easily manipulated, and can be had in angular shapes, an advantage, especially when canals have to be drilled in the longitudinal direction of the bone stems.

I have likewise designed a special instrument for carrying out boring operations. In this instrument the ordinary straight shank is inserted into a guiding device designed so that the shank and drill are guided in such a way that the holes drilled through the bone will lie radially in one and the same plane (Fig. 4). By means of a specially shaped chisel with an angular edge, the "angle-osteotome" (Fig. 5), the bone is cut through in the plane of the drilled holes. The ends of the bone cut through thus have uneven surfaces, and this factor may be of advantage when carrying out distractions. Moreover, the soft parts can be better preserved by this method than if the Gigli saw is used. The drilling apparatus makes only very slight movements in the soft parts, and in view of the ease and facility with which the shank can be handled, the hand quickly and easily senses when the drill has passed through the walls of the bone, so that the drill can be withdrawn before it has had time to injure the soft parts. In this form of osteotomy, the periosteum need be removed only on that side which faces the wound, and the marrow is not destroyed since the material inserted enters the medullary cavity only slightly, and cannot very well injure the endosteum. If the graft is spongy, this will facilitate the growth of the vesiculated connective tissue.

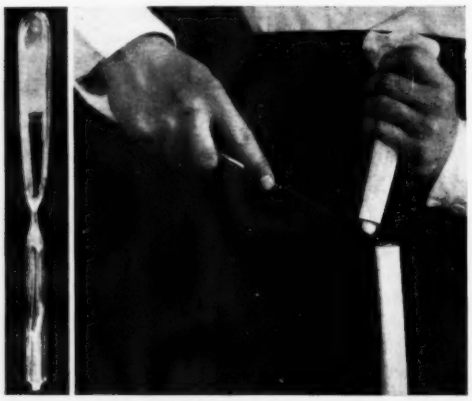


Fig. 3. a, left. Guide lever. An instrument resembling a mortise chisel, bow shaped cross section and chisel shaped at the end. b, After the graft has been fitted into the medullary canal of one bone end, it is guided by means of a leverage movement of the guide lever toward the medullary canal of the other bone end.

The aforesaid drilling machines are, as is well known, driven by electric motors, which are very highly perfected for their purpose. They are extremely reliable, run almost noiselessly, and are powerful enough for drilling into bone. They can also rotate the drills in either direction, so that, if these get stuck in the drill hole, they can be easily released. For the shanks I have designed drills of a particular type, with the cutting edge ground into milling cutters (Fig. 4).

In my research in grafting I have come to the conclusion that, in transplantation operations, soft tissues should be treated with the utmost care, since it is these tissues that produce the new bone and give it nourishment. The soft parts are, therefore, kept apart by specially designed straight obtuse angled bone spatulas (Fig. 6), the periosteum being removed from the bone to a very slight extent. The periosteum should, first of all, not be separated from its own soft tissues, which convey nourishment, and the marrow should be protected to the utmost possible degree.

The spherical graft can easily be made and standardized. The bone graft can also be made lentil shaped, conical, discoid or meniscoid, or

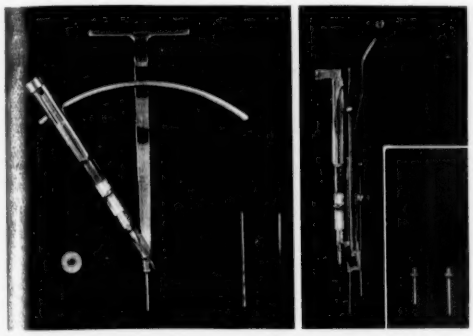


Fig. 4. Guide mechanism for the handle and drill. All the necessary parts are shown in the figure. The drills are of special design.

may be grooved or of an altogether irregular shape, and yet fulfil its purpose of uniting and keeping together the ends of the bones. Sometimes it may happen that one cannot determine the shape of the graft until the wound is open. For that reason a so called technique-motor, used in dentistry, provided with a circular saw and milling cutter specially made for that purpose should always be at hand. Even mortise chisels and vices, suitably fitted up on a table or bench, should be available. If these tools are at hand, and if one has become familiar with their use, the operations will not be difficult to carry out.

The tools and instruments mentioned are practicable and necessary also in other forms of bone implantation and bone plastic surgery.

The risk of pseudarthroses exists, of course, in this as in other methods, but very likely the risk is less, since a lateral displacement of the ends of the bones is here more safely prevented. To diminish the risk of pseudarthrosis arising, the external fixation, which is meant to prevent any movement between the ends of the bones in other directions, must be effective for about 10 weeks after the operation. During this period the new bone, as a rule, develops enough to obtain sufficient strength. The occurrence of infection during operation must be excluded with absolute certainty.

Case 1. No. 6633. Youth, 17 years of age. September 9, 1931, patient had a resection of the ankle joint for tuberculosis of the ankle. At operation, the resected bone was replaced by a disc of os purum spongiosum, which was inserted between the resection surfaces. The wound healed *per primam*. The patient was allowed to get up 3 months after operation, with a plaster-of-paris cast. February 29, 1932, a leather bandage was applied. This was removed on August 1, 1932. Good functional and anatomic healing was present. To assure that the implanted bone disc did not collapse, a bone pin of a less

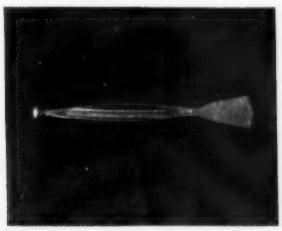


Fig. 5. Angular osteotome. The angular edge points downward, the handle upward.

easily dissoluble material was driven in, at the operation, frontally, through the fibula and talus (Figs. 7 and 8, *1*). As is seen, the bone pin is neither bent nor fractured.

Case 2. No. 6937. Boy, aged 13 years. Patient had suffered a tuberculous coxitis which had healed with flexion and adduction contractions. August 4, 1932, a subtrochanteric osteotomy was done. The ends of the bones, on osteotomy, were united by inserting, by means of the "guide lever," a sphere of os purum compactum into the medullary canals of the ends of the bones. Roentgenograms, taken 97 and 295 days after the operation (Fig. 9), show that the healing of the bone is extremely good peripherally around the sphere, and that the latter is being gradually resorbed.

Case 3. No. 6840. Man, 37 years old. December 22, 1931. A resection of the knee joint was done for tuberculosis. After resection, the ends of the bones were joined together by driving in a tongue shaped piece of os purum (Fig. 10, *1*). Primary healing took place. According to roentgenograms taken 610 days (1 year 8 months) after operation, progressive anatomical transformation of the graft has taken place (Fig. 10).

Case 4. No. 6846. E. B., girl, 13 years old. The diagnosis in this case was genu varum after tuberculous coxitis. March 18, 1933, operation consisting of osteotomia infracondylaris tibiæ and bone grafting was done. After an ordinary cut in the soft part was made, the osteotomy was performed by means of a drilling apparatus and angle osteotome. The bone ends were parted with a distractor, and small bits of os purum were interposed between the medial parts of the bone ends, so as to obtain the proper position between them. The periosteum was

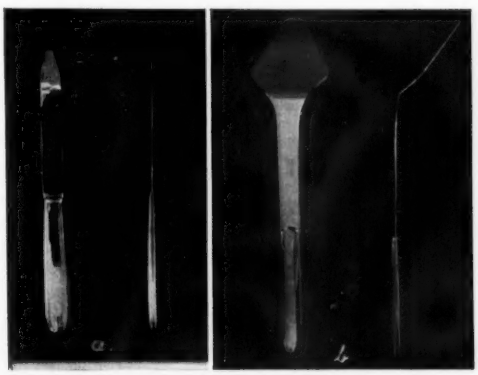
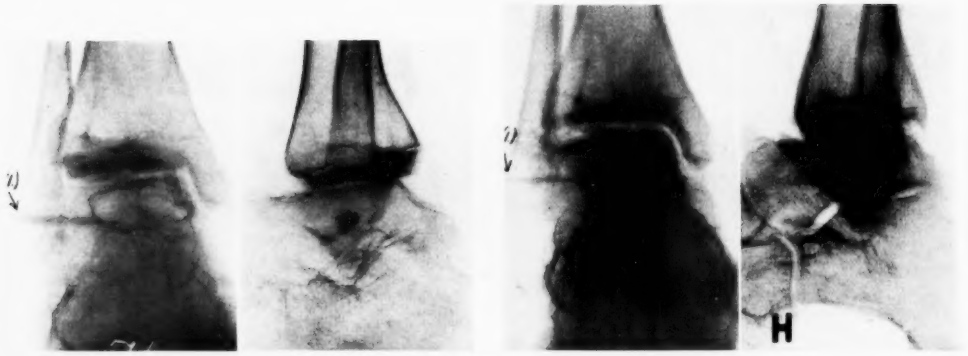


Fig. 6. a, Straight steel spatulas. b, Obtuse angled steel spatulas.



Figs. 7 and 8. Roentgenograms in Case 1.

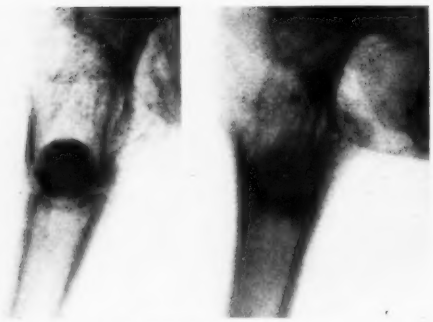


Fig. 9. Roentgenograms in Case 2.

Fig. 10. Roentgenograms in Case 3.

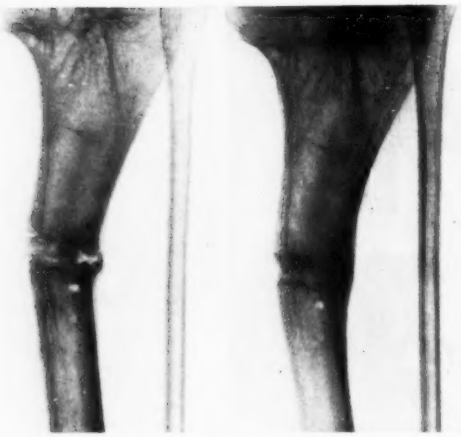


Fig. 11. Roentgenograms in Case 4.

sutured, and also the other soft parts. A fenestrated circular, plaster-of-paris cast was applied around the thigh, shin, and foot. Primary healing took place. After 8 weeks the patient was able to be out of bed with a plaster cast on. Figure 11 shows roentgenograms on the day after the operation and 202 days (about 6½ months) after the operation.

SUMMARY

"Interpositional osteosynthesis" aims at the restoration of bone in defects, the result of osteotomy, resection of bones and joints, fractures, etc. For this purpose bone grafts, specially shaped so as to prevent or impede lateral or longitudinal dislocation between the bone ends are used. Dislocation toward the axis and periphery is, as a rule, prevented by externally applied surgical or orthopedic fixation devices.

As interpositional material, bone is used which by a special technique, has been properly freed of the soft tissues. This bone I have called *os purum*. The graft may be made any shape—spherical, lentoid, conical, discoid, clavate, linguiform, or any irregular form or shape.

Osteosynthesis is carried out by means of instruments especially designed for bone grafting. Among others there are the distractors, guide levers, bone spatulas, and specially arranged drilling machines similar to the type employed in dentistry.

Osteotomy is performed by means of a specially designed and constructed osteotome. "The angular osteotome," after the bone has been pierced in several places, is driven through the bone. With a guiding apparatus designed for shank and drill the holes are made radially in one and the same plane through the bone.

In the cases in which the method has been used, the healing of the wound has been primary and the bone grafts have been found capable of supporting, without collapsing, the mechanical strain to which they have been subjected. Moreover, the roentgenograms show that the epiphyseal grafts after 200 to 300 days after implantation begin to show signs of newly developed bone structure, and consequently, of reconstruction of bone, whereas the diaphyseal grafts, which are inserted into the medullary canal, sequestrate and dissolve after a comparatively short period of time has elapsed, while the regeneration of bone proceeds mainly between the ends of the osteotomized bones.

As in the comminuted fracture, a fragment of bone may prevent reposition and cause the fixation of the ends of the bones in a wrong position, so it is possible, by means of interposition in osteotomy, in bone and joint resection, in fracture, etc., to obtain reposition and fixation of the ends of the bone in a calculated, predetermined position. This is of importance, especially in those cases of osteotomy in which fixation after reposition is frequently never obtained, or is accomplished only with great difficulty merely by aids.

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BENIGN STRICTURE OF THE INTESTINE DUE TO IRRADIATION OF CARCINOMA OF THE CERVIX UTERI

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IN a series of 422 patients with cervical carcinoma who have received irradiation therapy at the Cleveland Clinic, there have been 6 cases (incidence 1.4 per cent) of benign stricture of the intestine which might easily have been confused with metastatic carcinoma. Subsequent to the irradiation therapy no evidence of carcinoma was found, and judging by present day standards, none of these patients received excessive irradiation. Since similar methods of irradiation therapy are in general use, it seems probable that the incidence of this lesion is greater elsewhere as well as here, than the literature would lead one to believe. And if similar cases have been attributed to metastases in the past, the mortality statistics relating to metastases from cervical carcinoma are open to question.

The present study directs attention to this benign lesion as a clinical entity, and offers suggestions for its prevention, the results of which will be reported in a later communication.

It should be emphasized that a patient who develops unusual abdominal symptoms, particularly if they simulate intestinal obstruction, several months or even years following irradiation therapy, may have an irradiation stricture of the intestine, and may be restored to normal health by a resection of the lesion. Before the disability is attributed to metastasis, a re-examination should eliminate the possibility of this curable complication. At least sigmoidoscopic and colon roentgen examinations should be done, and a careful roentgen study of the small intestine may be advisable, provided the obstruction is not complete. Exploratory operation is warranted, particularly on patients presenting evidence of intestinal obstruction in whom there is no remaining evidence of carcinoma in the pelvis.

Of the 6 cases reported here, 5 of the benign strictures occurred in the sigmoid colon and 1 in a lower loop of small intestine.

CASE REPORTS

CASE 1. A woman, aged 60 years, when first examined, had a carcinoma of the cervix uteri (stage 2), extending into the broad ligament. Biopsy showed that the growth was a squamous cell carcinoma, and the patient was treated by irradiation with radium and roentgen-rays.[1]

Follow-up examinations had shown no evidence of malignant disease, and the patient had been in excellent health for over 2 years after the last radium treatment. Then she began to have unusual constipation, which became progressively more severe, and at the time of readmission, a few weeks after its onset, she had symptoms and signs of intestinal obstruction. Proctoscopic examination was negative, and no blood or mucus was seen in the bowel. Roentgen examination of the colon revealed an obstructing lesion in the sigmoid colon, which was believed to be due to carcinoma (Fig. 1). At operation, the lesion was found to have the characteristics of a benign stricture. There were bands of adhesions encircling the sigmoid colon at the site of the lesion and these were attached to the fundus of the uterus (Fig. 2). The adhesions were severed, this portion of the colon was resected, and an end-to-end anastomosis was made. The pathological diagnosis was chronic inflammation. The patient recovered well from the operation, and has reported normal health on numerous occasions during the 2½ years since the resection was performed.

CASE 2. The patient, aged 52 years, had had a pelvic abscess years previously, and came to the Clinic because of pelvic symptoms. The cervix uteri was firm, enlarged, and nodular, especially on the right side, and bled easily. There was no thickening in the broad ligaments. Squamous cell carcinoma was revealed by biopsy and radium and roentgen irradiation therapy was administered.[2]

For a year and a half after the irradiation therapy, follow-up examinations had shown no evidence of disease, and the patient had been in excellent health. Then she started to have severe pains in the bladder, associated with some blood in the urine. These symptoms persisted for 3 weeks. Cystoscopic examination when the patient returned to the Clinic, revealed several submucous hæmorrhages on the posterior wall of the bladder, in the center of which was a white, irregular area about 2.5 centimeters in diameter. Subsequent examinations showed the development of a definite ulcer in the irregular area mentioned. One year following the initial cystoscopic examination, the ulcer had disappeared completely except for a small area of submucous hæmorrhage due to separation of the slough a few days previously.

Approximately 1 year and 9 months subsequent to the irradiation therapy, the patient began to have unusual abdominal symptoms, simulating intestinal obstruction. Roentgen examination of the colon showed no obstruction at the time of the onset of these symptoms. No further roentgen studies were made. The initial attack soon subsided, but 2 months later there was a recurrent attack which was more severe, and operation was performed.

[1] One tube containing 170 millicuries of radon was inserted into the cavity of the uterus and cervical canal for 12 hours, producing a total irradiation of 2,040 millicurie hours. Three days later, roentgen therapy was started. Two months later a second radium treatment was administered to the cervix, 220 millicuries of radon in four tubes being placed against the cervix for 10 hours, totaling 2,200 millicurie hours, or a total for the two radium treatments of approximately 4,240 millicurie hours. The actual amount of radiation received represents about 3 per cent less than these figures, when calculated according to the time the radon is in place.

[2] Two tubes containing 305 millicuries of radon were inserted into the uterus and cervix and two tubes containing 140 millicuries of radon were placed against the cervix for 6½ hours, producing a total irradiation of approximately 2,759 millicurie hours. Twelve days later roentgen therapy was started.

Fig. 1. Example of benign stricture of sigmoid colon simulating annular carcinoma.

Fig. 2. Pathological specimen showing benign stricture of sigmoid colon. (Case 1.)

There was an old inflammatory process in the uterine tubes, but no evidence of carcinoma could be found. About 25 centimeters proximal to the rectum there was a definite, almost complete obstruction of the sigmoid colon. It seemed as if there were a cicatricial band in the bowel wall, with very little inflammatory reaction outside. Resection was considered, but it was deemed more advisable to make an anastomosis around the obstruction, particularly in view of the fact that the sigmoid colon was unusually long. A side-to-side anastomosis was done. The last follow-up letter from the patient, 5 years after the operation, states that she is in normal health.

CASE 3. The patient, aged 58 years, had a carcinoma of the cervix uteri, involving chiefly the posterior lip and the posterior vaginal wall (stage 2). The pathological diagnosis was squamous cell carcinoma. Radium therapy was followed by roentgen irradiation.[1]

For 5 months the patient showed satisfactory progress, but did not return for the usual subsequent examinations. Later, in a letter from the patient's husband who was a physician, it was learned that the patient had been confined to bed for a month because of abdominal pain, nausea, and pronounced vomiting. Examination revealed no evidence of carcinoma in the cervix or in neighboring structures. Death followed 1 month later. Complete autopsy was not permitted but examination of the abdominal contents revealed an inflammatory stricture of the lower small intestine, causing a definite obstruction. The exact relation of this area to the uterus was not stated, but examination of this area of the intestine and the uterus, after removal from the abdomen, revealed adhesions on the peritoneal surfaces of both.

From these findings it may be inferred that the stricture of the small intestine involved an area adjoining the uterus, that fibrous adhesions formed between the two, and that the cause of death (since no other cause was considered or found) was severe toxæmia, resulting from small intestinal obstruction.

CASE 4. The patient, 41 years of age, had an enlarged cervix uteri which was bleeding and ulcerated. The principal involvement was inside the cervix, extending into the uterus and outward through the cervix, lateral to the external os (stage 1). The biopsy showed squamous cell carcinoma. Radium and roentgen therapy was administered.[2]

The usual transitory sequelæ immediately following these treatments were prolonged in this case. For 6 months, the patient complained of loose stools containing unusual quantities of mucus. The following month there was marked constipation, and after a period of 11 days without a stool, the patient suffered from considerable abdominal distention, and was re-admitted to the hospital with a diagnosis of intestinal obstruction. Follow-up examinations had shown no evidence of recurrence of the malignant growth in the cervix and no evidence of pelvic metastasis. Proctoscopic examinations had shown no evidence of disease. Laparotomy was not done at this time because her symptoms were relieved by the use of enemas and hot fomentations to the abdomen.

She was re-admitted to the hospital at 2 and 6 month intervals subsequently. An attempted barium enema was expelled as soon as it had reached the sigmoid colon, apparently indicating obstruction at this level.

A cæcostomy was done and a large tube was inserted into the dilated ascending colon for irrigations, 15 months after irradiation therapy. Later, a colon roentgen examination, during which the barium suspension was injected through the colostomy tube, revealed a definite obstructing lesion in the sigmoid colon. At the subsequent operation,

[1] One tube containing 118 millicuries of radon was placed in the cervix, and another tube containing 177 millicuries of radon was placed against the posterior lip of the cervix, for 10 hours, or a total of approximately 2,950 millicurie hours. One and a half months later roentgen therapy was administered.

[2] One tube containing 106 millicuries of radon was placed into the fundus of the uterus, one tube containing 247 millicuries of radon was placed in the cervix, and four tubes containing 142 millicuries were placed against the cervix, for 8 hours, or a total of approximately 3,960 millicurie hours. One month later roentgen therapy was administered.

performed recently, the lesion proved to be a benign stricture causing complete obstruction. This portion of the colon was resected, and an end-to-end anastomosis was made. The patient's recovery following the operation was uneventful.

CASE 5. The patient, 50 years of age, had a diffuse carcinoma of the cervix uteri, involving chiefly the cervical canal (stage 1). Squamous cell carcinoma was revealed by biopsy and the patient was treated by irradiation.[1]

Subsequent examinations revealed satisfactory progress, and the patient was in good health except for an attack of gall-stone colic. Approximately 3 years following irradiation therapy, she stated (for the first time) that she had had some blood in the stools off and on during the previous year, which she attributed to hæmorrhoids. Unusual constipation was also present. Pelvic and proctoscopic examinations showed nothing except the hæmorrhoids, and these were treated by the injection method. A colon roentgen examination, however, revealed an annular filling defect in the sigmoid colon, and re-examination 1 month later revealed the same finding. Bleeding continued at intervals and in one instance there was a cupful of blood clots.

At operation (3¼ years following irradiation therapy), the lesion proved to be a benign stricture. This portion of the colon was resected and an end-to-end anastomosis was made. Death from local peritonitis followed 15 days after the operation.

CASE 6. The patient, aged 59 years, suffered from a carcinoma of the cervix uteri, involving chiefly the anterior lip of the cervix and extending into the vaginal wall (stage 2). The lesion, as determined by biopsy, was a squamous cell carcinoma. The patient was treated by radium irradiation[2] but received *no roentgen therapy.*

The patient made satisfactory progress but complained of slight constipation which was unusual for her. Seven months following radium irradiation she stated that during the past few weeks the constipation had become more severe and that she had passed darkened blood, blood clots, and mucus by rectum, associated with cramp-like abdominal pains. Pelvic examination showed nothing of significance, but roentgen examination of the colon revealed a conical, fixed, concentric narrowing in the mid-sigmoid area, believed to be due to an irradiation stricture. At operation the stricture was immediately behind the fundus of the uterus. It appeared anæmic as compared with the remainder of the sigmoid colon. A cæcostomy was done, and 1 month later a resection of the lesion, and end-to-end anastomosis. The patient was discharged from the hospital 1 month after operation, having normal stools.

The lesion. In all the cases herein reported, at operation the lesion was found to have the appearance and consistency of an annular fibrous thickening in a localized segment of intestine, associated with a varying constriction of its lumen. "The lesion appeared to be a cicatricial band in the bowel wall" (operative notes). The cause of the varying degrees of intestinal obstruction elicited clinically was obvious. The lesion ma lie adjacent to the uterus, and be fixed to the lat ter by adhesions. If the lesion is in the sigmoi colon there may be a somewhat redundant dista loop of sigmoid colon, extending to the right sid of the pelvis, distal to the involved fixed segment Other evidence of intestinal obstruction, such a dilatation of the intestine proximal to the point o obstruction, depends, of course, on the degree o obstruction.

The pathological changes found in the resecte lesions are similar to those described by Desjar dins in a review of the literature to 1931, on th "Action of Roentgen Rays and Radium on th Gastro-Intestinal Tract, Experimental Data and Clinical Radiotherapy." The cases in this report, however, may represent a later stage of the inflammatory process in which annular fibrosis with narrowing of the lumen was the predominant finding. In addition to the intestinal lesion, in Case 2 there was a late bladder ulcer, which was first ascribed to carcinomatous extension. The importance of recognizing the bladder lesions resulting from irradiation has been emphasized by Healy and by Ward and others.

Ulceration may or may not be present at the time the involved segment of intestine is removed. The chronic inflammatory changes found in all lesions were a contracted lumen and thickening of the wall of the intestine, due to infiltration with granulation tissue, plasma cells, eosinophiles, and to varying degrees of replacement by fibrous tissue, particularly in the older lesions. Any stage of chronic inflammation may be found, but annular fibrosis resulting in a narrowed lumen was the predominant finding in the cases herein reported. If ulceration is present, it may involve only the epithelium of the mucosa or it may extend through all the layers of the intestine into the adjacent mesenteric fat. No evidence of acute perforation into the peritoneal cavity was found in this series of cases.

Diagnosis of the lesion. An irradiation stricture of the intestine should be suspected in any woman who develops unusual abdominal symptoms, particularly if they simulate intestinal obstruction several months or even years subsequent to irradiation therapy for cervical carcinoma. This is especially true if there is no remaining evidence of carcinoma in the pelvis. The history relative to bowel function is of first importance. Minute inquiry concerning the immediate post-radiation sequelæ must be made. All 5 patients with sigmoid lesions, herein reported, had tenesmus, diarrhœa, and passed mucus and blood in the stool for 3 weeks, or longer, immediately following th

[1] Two tubes containing 244 millicuries of radon were inserted, one in the cervix and one against the cervix, for 10 hours, or a total of approximately 2,440 millicurie hours. One month later, roentgen therapy was administered.

[2] The tube containing 266 millicuries of radon was inserted into the cervical canal and ten radium needles, each containing 10 milligrams of radium were inserted into the carcinomatous mass, approximately 1 centimeter apart; and one tube containing 107 millicuries of radon was placed against the anterior lip of the cervix, a total of 373 millicuries of radon and 100 milligrams of radium for 7½ hours, equivalent to approximately 3,729 milligram hours of radium.

irradiation therapy. This is in contrast to the usual milder transitory sequelæ which subside within a week or 10 days after irradiation therapy. In the patient in whom an irradiation stricture is forming, unusual constipation supervenes sooner or later, along with other symptoms of varying degrees of intestinal obstruction. Intestinal hemorrhage may be the chief complaint.

A sigmoidoscopic examination may not reach the lesion in patients having a sigmoid lesion, because of unusual fixation of the involved area, or an unusually redundant sigmoid colon distal to the lesion. The sigmoidoscope failed to reveal the stricture in the 5 patients reported here.

The colon roentgen examination was the most important single means of revealing the lesion in the sigmoid colon. In the cases in which the obstruction was not complete, the lesion was represented by an annular filling defect, simulating the infiltrating type of carcinoma. In contradistinction to the latter, however, the benign stricture usually had an hour-glass deformity, was usually fixed in position, although of small size, and it had a more gradual line of demarcation between the normal and abnormal tissue than is usually seen in carcinomatous lesions of this area. The lumen of the intestine usually had a conical shape on either side of the lesion, the apices of the two converging cones coming together and representing the stricture. A redundant loop of sigmoid colon, distal to the involved area, may make the examination difficult. In this type of case, in addition to the fluoroscopic examination, it may be necessary to have roentgenograms made with the patient in several positions, only sufficient barium suspension to fill the sigmoid colon being used. And after the expulsion of the barium suspension from the sigmoid colon, an air injection may be done and stereoscopic films exposed. In the usual examination, in which the film is exposed after distention of the entire colon with barium suspension, regurgitated barium in the terminal ileum may make roentgenographic demonstration of the lesion impossible. An ulcerating lesion will have the characteristic irregular, jagged luminal contour and asymmetrical channel. In the case of obstruction in the small intestine, plain or stereoscopic films of abdomen may suffice to establish approximate area involved, or, if necessary, a small amount of barium suspension by mouth, followed by study of barium in small intestine at appropriate intervals, is usually not contra-indicated.

TECHNIQUE OF IRRADIATION THERAPY

Five of the six patients had received both radium and roentgen irradiation. The radium was administered by Dr. Thomas E. Jones and the roentgen therapy by Dr. U. V. Portmann. In Case 6, the patient had only radium irradiation. The dosage of radium varied from 2,440 millicurie hours to 4,240 millicurie hours. Tubes of radon having 1.5 millimeters of brass filtration enclosed in 2 millimeters of rubber were used in all cases. In addition, in Case 6, radium needles were inserted into the carcinomatous tissue. Roentgen therapy was administered through four portals, suprapubic, right iliopubic, left iliopubic, and postsacral, each portal alternately receiving 50 per cent of a skin unit dose at a time, and the entire course in each instance was given in 5 to 7 days. The skin unit dose was 800 roentgens and the estimated 10 centimeter depth dose was 30 to 40 per cent, a potential of 200 kilovolts being used, 5 to 8 milliamperes with filtration varying from 0.5 to 1.0 millimeter copper and 1 millimeter of aluminum and varying sized portals at 50 centimeters focal skin distance, depending on the thickness of the patient. The total calculated roentgen dose about the cervix was approximately 800 roentgens.

Radium and roentgen-rays in the etiology of the lesion. According to Glasser, the depth penetration of one tube of radon having the filtration used in these cases, when a depth of 1 centimeter is considered to receive a 100 per cent dose, or approximately 10 erythema units, is as follows: a depth penetration to 2 centimeters will receive only 27 per cent (2.7 erythema units); to 3 centimeters, only 12 per cent; to 4 centimeters, only 7 per cent; and to 5 centimeters, only 4 per cent (0.4 erythema units). It is obvious, therefore, that a segment of intestine to be affected by the radium irradiation must lie very close to the area treated, and must remain in that position more or less constantly during time radium is in place.

The following table is representative of the roentgen therapy received by each of the 5 patients, showing the distribution of the irradiation in the pelvis, according to Glasser's isodose charts (Table I and Fig. 3). These factors produce a homogeneous roentgen irradiation to the pelvic contents, and no one segment of the intestine in the pelvis should receive more irradiation than any other segment. If it is kept in mind that the last patient in the series received only radium therapy, it is logical to assume that in the 5 other patients who received both types of irradiation, roentgen therapy aggravated a condition already started by the radium.

PREVENTION OF THE COMPLICATION

If an irradiation stricture develops in a localized segment of intestine because this segment, during

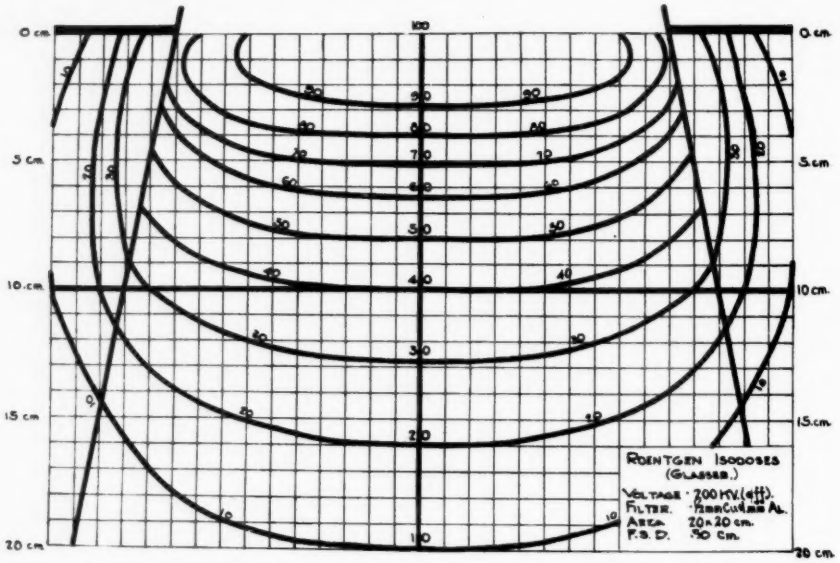

Fig. 3. Isodose chart (Glasser) showing depth penetration of roentgen radiation.

the time of the radium irradiation, remains constantly in one position, adjacent to the area being treated, the lesion should be prevented if the position of this segment can be changed at intervals during the time the radium is in place. Changing the position of a lower loop of intestine without dislodging the radium may be difficult to accomplish.

During roentgen examinations, the position of redundant loops of intestine change appreciably when the position of the patient changes. The most pronounced alteration is observed during the examination of a freely movable redundant sigmoid colon, when the patient is moved from a horizontal to a Trendelenburg position. Changing the position of the patient at intervals during the time of the radium therapy should prevent overirradiation of any one redundant segment of intestine, unless that segment is fixed in position (pelvic inflammation?) at the time of the irradiation. The radium inserted into the cervical canal would not be dislodged during such a procedure, provided the usual thorough packing of the vagina were done. The procedure would seem to be especially indicated when the radium is inserted high up into the fundus of the uterus. When the radium is placed against the cervix or inserted into the cervical tissue (needles), keeping the patient in a constant moderate Trendelenburg position would aid in the maintenance of the proper position of the radium, and at the same time should allow sufficient area between the radium and the intestine to prevent the development of the lesion under consideration. If the intra-uterine application of radium is made separately and not when other types of applications are made, the maximum prevention should be possible, so far as changing the position of the patient during radium therapy is concerned.

If continued peristaltic activity of the intestine could be obtained during the time of irradiation therapy, this also might be a means of changing the position of redundant loops of intestine. A

TABLE I

	Cervix	Glands, 4 cm. from cervix	Bowel, 4 cm. from cervix
Field 1 (Suprapubic)			
Skin dose	700 r	700 r	700 r
Depth	40 %	40 %	30 %
Depth dose	280 r	280 r	210 r
Field 2 (Right iliopubic)			
Skin dose	400 r	400 r	400 r
Depth	25 %	25 %	30 %
Depth dose	100 r	100 r	120 r
Field 3 (Left iliopubic)			
Skin dose	400 r	400 r	400 r
Depth	40 %	35 %	20 %
Depth dose	160 r	140 r	80 r
Field 4 (post-sacral)			
Skin dose	800 r	800 r	800 r
Depth	40 %	40 %	55 %
Depth dose	320 r	320 r	440 r
Total depth dose	800 r	840 r	850 r

medicament, such as pitressin, administered after the usual preparation of a thorough emptying of the intestine, might produce the desired effect. Keeping the tip of a flexible colon tube in the sigmoid colon (analogous to the usual procedure of keeping a catheter in the bladder) during the time the radium is applied, in the attempt to prevent any accumulation of gas in this area, might also be helpful.

CONCLUSIONS

1. In a series of 422 cases of cervical carcinoma in which irradiation therapy was administered, 6 patients presented the late complication of a benign stricture of the intestine. These cases might easily have been attributed mistakenly to metastatic carcinoma.

2. A patient having this lesion may be restored to normal health by surgical intervention.

3. A colon roentgen examination was the most important single pre-operative diagnostic means of revealing the presence of the sigmoid lesions.

4. It appears logical that this complication may be prevented without altering the principles of the well proved present day efficacious irradiation therapy of cervical cancer. This rare complication (incidence 1.4 per cent in this series of cases), when treated so successfully by surgical intervention, should not constitute a retarding influence on such therapy.

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VASCULAR DISEASE OF THE LOWER EXTREMITIES[1]

A Review of Amputation Criteria

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AMPUTATION criteria have been fairly well established for those emergencies which threaten the life of a previously normal limb. Prosthetic, mechanical, bacterial, neurogenic, hormonal, and direct traumatic factors as well as the acute vascular changes are all taken into consideration. When proper evaluation of each has been made, a decision as to the appropriate time, manner, and level of amputation can readily be reached.

The problem is more difficult, however, when it involves a limb already the seat of vascular disease. Here, in addition to evaluating all the factors mentioned, an appraisal must be made of the extent of vascular damage previously incurred. The amount of collateral compensation for this damage must be discounted, and the remainder (which represents the true vascular deficiency), added to the limb risk.

This is not an easy task. But some assistance is rendered by what modern knowledge offers covering the pathogenesis and progress of vascular occlusion in these cases, and by a multiplicity of clinical tests which offer at least inferential evidence of the vascular condition of the extremity. An analysis of the problem in the light of this knowledge and with the aid of some of these tests, it was thought, might be of some value in helping define the amputation criteria in these cases.

THROMBO-ANGIITIS OBLITERANS

Thrombo-angiitis obliterans is an inflammatory condition of vascular walls, of unknown etiology, associated with the formation of occlusive thrombi. As yet there is no proof that any specific bacterium or toxin is involved. Neubuerger in fact explains the entire pathogenesis of the condition on the basis of Ricker's hypothesis. According to this hypothesis, whatever noxi are responsible for the disease act by setting up local neurovascular instabilities. Arteriolar spastic crises end in paralysis and dilatation with slowing of the blood stream. The various organic changes in the vessel walls are secondary to varying degrees of retardation of the nutritional flow. On this basis, in pathogenesis, at any rate, thrombo-angiitis is only a slightly milder but more tenacious Raynaud's disease.

The disease appears and subsides. The vesse wall changes and occlusive thromboses which before long result, are closely followed by the canalization and organization of the thrombi, and by the opening up of collateral channels; the amount of actual vascular deficiency which remains, depends on the relative speed of the two processes (10, 37, 38, 46, 51, 57).

The disease is usually slow in its progress. It occurs characteristically in relatively young individuals who start with an ample capacity for the development of collateral circulation and for the thrombus re-canalization. The disease process, itself, interferes in no way with the development of collaterals. At the onset at least, it is limited and focal in its attack so that only short segments of thrombi have to be re-canalized and only short collateral circumductions provided. Compensation is readily made. As the attack subsides, circulatory efficiency is re-established with only a slight withdrawal from the available collateral supply. At best, however, the disease is remittent. With each attack, more of the main channels are occluded and more of the collateral channels are opened up. With its varying intermissions, the disease progresses relentlessly. With each attack, the margin of safety shrinks. Yet if the process be slow enough and the patient young, the main channels may become totally occluded and the life of the limb be maintained by the extensive opening up of collateral channels characteristic of this disease. Barely enough blood flows, however, through these vicarious channels to maintain life in the part. The demand for more blood under exercise of the limb finally cannot be met and ischæmic cramps hinder activity. The increment required for the healing of minor wounds cannot be supplied and they fail to heal. With all collaterals widely dilated, further circulatory damage cannot be compensated and gangrene develops.

Sometimes the disease takes a more rapid course. Attacks of migratory thrombophlebitis follow closely one upon another with short or no healing intervals. Sometimes it starts in older individuals or is complicated by arteriosclerosis. Under these circumstances, little collateral compensation develops and even less extensive vascular occlusion can quickly lead to gangrene.

[1] From the Department of Surgery of Northwestern University Medical School. Study made on patients of Cook County Hospital and Wesley Memorial Hospital. Read before the Chicago Surgical Society, March 2, 1934.

The disease is nearly always bilateral. When manifest in only one leg, it is almost certain to be latent or potential in the other, and sooner or later, may be expected there also.

When the question of amputation is raised, the first problem is to determine just how extensive the arterial blockage has been and how extensive the collateral circulation in compensation. This may be determined by various clinical observations and by certain special tests. There is no absolute criterion of the circulatory efficiency of a limb, but by a combination of several different types of observation, a fairly reliable estimate may be obtained.

From an accurate history alone some inference can be drawn concerning the circulatory condition of the limb. The age of the patient gives the likelihood for complication with arteriosclerosis and some idea of the collateral potential. The duration of symptoms and the relation of periods of activity and attacks of thrombophlebitis with intervals of remission and recovery, give an account of the various inroads on the vascular supply, the extent of probable compensation, and the available collateral supply left. The severity of current symptoms is roughly proportional to the circulatory deficit.

The general appearance of the limb in the horizontal position is of some importance. To what level normal color is seen and the extent and intensity of anæmia and rubor are to be noted. The general nutrition of the limb, the color changes of chronic stasis, scaling, fissures, calluses, nail changes are all to be considered. All these denote total circulatory deficiency of which ulcers and finally gangrene are the end stages. The extent of the gangrene and its demarcation are to be noted, but this observation is notoriously unreliable in determining the degree of circulatory deficiency of the whole limb (25). It only specifies the degree of local deficit. With a large area of gangrene, the rest of the limb may be fairly well supplied with blood. With little or no gangrene, severe pain, color, nutritional and other changes may show the whole limb to be fairly devascularized. Usually sharp demarcation speaks for the excellent development of collaterals down to the level of gangrene (Meleney) but this sign of circulatory efficiency would be invalidated by infection. Finally the total extent of skin gangrene portrays only inaccurately the extent of deep gangrene which may be considerably greater or smaller.

Of greater importance than the simple appearance of the limb is the extent of the anæmia which appears on elevation, and the rubor which appears on dependency. The levels to which these rise are

Fig. 1. Normal leg. Vessels injected with barium sulphate under normal systolic blood pressure of the patient. Note smooth contour of main vessels and moderate collateral supply.

the levels of circulatory sufficiency under static strain. The intensity of these changes and the angle of circulatory sufficiency (Buerger) give a fair estimate of the degree of deficiency. These signs, however, do not determine the level of circulatory sufficiency under muscular strain. This can be inferred only from the symptomatology. Nor do they determine the circulatory sufficiency under the strain of healing. This can be guessed or determined only vaguely from the history of previous wound healing difficulties.

The level of abrupt temperature change is of great assistance. The limbs are left alone for 15 minutes, then covered with the bed clothes for 15 minutes (58). There is a normal, acralward gradual decrease in skin warmth but there is never an abrupt change unless there has been vascular occlusion without adequate collateral compensation. The temperature change level may be determined roughly by the hand or by a clinical skin thermometer or more accurately by the thermocouple (12).

These observations as well as most of those which follow, record the total circulatory status, i.e., vascular obstruction minus collateral compensation. The level of actual main vascular obstruc-

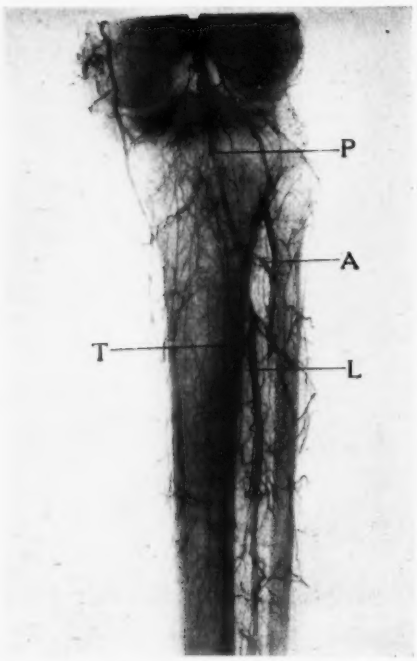

Fig. 2. Case of thrombo-angiitis obliterans. Showing the patchy irregularities along the popliteal, *P*, and anterior, *A*, and posterior, *T*, tibial arteries, and the large and numberous collateral vessels. The peroneal artery, *L*, is well preserved and larger than normal. (Photograph loaned by Dr. Frank Meleney.)

tion can be estimated by palpation of the main vessels. Routinely, the dorsalis pedis, posterior tibial, popliteal, and femoral should be palpated.

It is possible, however, for all these vessels to be pulsatile, yet an early Buerger's disease be detectable in the plantar vessels by plantar anæmia on elevation. Circulatory deficiency should not be dismissed on the basis of pulsatile vessels.

The chief difficulty with this palpatory sign, however, is that the main vessel pulsations are accessible to tactile perception only at a few widely separated points about the main joints. To obviate this difficulty and to obtain a more quantitatively accurate estimate of vascular pulsation, the Pachon oscillometer was devised (54, 61, 62). This may be applied at any segment of the limb and the total vascular pulsatility of that segment under varying external pressures determined and compared with the other limb or with the normal. At the level of main vascular occlusion there is decrease in the pulsation volume. This method unlike the tactile is not selective. The anterior tibial artery may be occluded just above the ankle. Yet if the posterior tibial dilate sufficiently in compensation the pulsation volume may be maintained. Even smaller collaterals may compensate for the decrease in pulsation volume caused by occlusion of the main channels.

For these reasons except in acute vascular obstruction, the Pachon oscillometer does not determine the exact level of occlusion. Its accuracy is inversely proportional to the extent of collateral development. Usually there is some decrease in pulsation volume at or a little below the point of main vessel occlusion. Pulsation continues, however, until the end of the pulsatile collateral supply is reached.

The oscillometer determines the level of pulsatile collateral supply. Beyond this level there is an oozing, non-pulsatile collateral supply which the machine does not register. This occult circulation between *O* of the instrument and the total cessation of arterial flow may be observed by decreasing the bag pressure in the non-pulsatile segments until a dusky red blush appears. This represents the first escape of oozing blood (Simpson). The non-pulsatile flow may be rich enough to keep the tissues alive and even bear the strain of postoperative healing. It may permit amputation below the level of *O* deflection of the Pachon oscillometer.

To determine the extent of this non-pulsatile but adequately vascularized zone, other methods are used. One of these is the McClure-Aldrich intracutaneous salt solution absorption test (Stern and Cohn): 0.2 cubic centimeter of 0.85 per cent sodium chloride is injected at 4 inch intervals down the limb. Normally, the wheal should remain for 60 minutes. In impending tissue œdema induced by circulatory deficiency, the absorption time is markedly reduced. The test is simple, painless, and gives a reliable estimate of skin circulation. It cannot be used where there is already an inflammatory, static, or nephritic œdema. Objections to it have been raised on the grounds that tissues which are the site of impending gangrene, should not be injured further by needle pricks. It does not seem that a hypodermic salt solution wheal would produce material injury.

Another similar method is the histamine flare test (20, 30). It depends on the universal anaphylactoid vasodilatory response, wherever there are capillaries to dilate. One-tenth cubic centimeter of 1:1000 histamine is injected intracutaneously at short intervals down the limb. There is at first a cyanotic flush, then a hyperæmic flare, and finally wheal development. If at a certain level a flare does not appear, amputation

must usually be done above this level. If a flare does appear (without regard to time interval), the skin circulation may be adequate for amputation, or may not be. The test has chiefly negative value, therefore, but is a good auxiliary sign. Clinically, its results have been found to be more accurate than those of the McClure-Aldrich test, but the injections hurt about as badly as a bee-bite. (Perlow has recently devised a method of rendering these injections painless. Novocain is added to the histamine solution to make a concentration of ½ per cent. We have tried this method with gratifying results. The novocain interferes in no way with the test, and completely prevents the pain.) Both of these skin tests are open to the objection that skin circulation may not be an accurate measure of muscle and bone circulation. The deeper structures may be non-viable beneath well nourished skin.

A direct study of the circulatory adequacy of the deeper structures may be obtained by the thermocouple and galvanometer method of Brooks and Jostes or by the calorimeter method of Stewart. These methods are too time consuming and cumbersome for routine clinical use.

X-rays are taken routinely. They may disclose areas of osteomyelitis and reveal the amount of arteriosclerosis present. The latter factor is of only moderate value because extensive sclerosis may be present with adequate collateral circulation or slight sclerosis with inadequate collaterals. Although the vessels may be easily and plainly visualized by X-ray, the degree of opacity to the X-ray does not always correspond to the patency of the vessels themselves. Direct visualization of the circulation in the affected extremity by injection of radio-opaque substances has also been recommended (Singleton, Pearse, 56), but is too heroic a method for general use. They are painful enough to necessitate nerve block anæsthesia for their induction. The effect of these substances on vessels already damaged by disease is not beyond suspicion. The Matas and Moszkowicz tests of inducing hyperæmic flush by temporary anæmia are open to the same objections (40).

In 90 to 95 per cent of the cases, simple clinical tests are sufficient to determine the level of adequate circulation. Palpation and the Pachon oscillometer determine the level of main vessel occlusion and the level of cessation of pulsatile collateral flow. The history of the case, the severity of symptoms, the appearance of the limb when horizontal, the skin temperature change level, and the histamine or salt solution tests give a fair estimate of the level to which the non-pulsatile collateral flow has been developed. Rubor on dependency and anæmia on elevation estimate the adequacy of the collateral circulation to static strain. The reaction of the limb under muscular activity gives an estimate of its adequacy under the strain of muscular exercise. The response of minor lesions to conservative treatment gives some estimate of the capacity of collaterals to provide for healing.

Fig. 3. Arteriosclerotic gangrene. Vessels injected. Note beading and irregularity of main vessels and paucity of collateral channels. Patient 64 years old.

With the total decrease in circulatory intensity determined, an estimate must be obtained of the amount of this decrease which is spastic and the amount organic. On this depends in some measure the types of pre-amputation procedures instituted. The spastic element may be differentiated and evaluated by instituting measures which paralyze vasomotor constriction (6, 13, 18, 21, 22, 48, 49). This may be done by immersing the part in a warm bath, by inducing a general fever with killed typhoid bacilli intravenously, by paravertebral block, spinal anæsthesia, general anæsthesia, peripheral nerve block or diathermy application to the cervical or lumbo-sacral regions. Of these, the best and most widely used method is that of

Fig. 4. Diabetic gangrene in a young adult. Note the beading and irregularity of the main vessels, but the supernormal richness in collateral development. The gangrene of the anterior third of the foot which developed here was on an infectious basis and did not depend on circulatory deficit.

peripheral nerve block. The rise of local skin temperature (and the increase in oscillometric excursion) after anæsthesia is an index of the amount of vasoconstriction responsible for the local circulatory deficiency. The remainder is the organic factor.

Before amputation is decided upon, unless the indication is urgent, some attempt should be made to improve the collateral circulation and to reduce the spastic element. Conservative management includes treatment of the local lesion, postural exercises (15), dry heat (60), saline or citrate solution in large quantities orally (32), subcutaneously, intravenously, or by duodenal gavage, diathermy and intermittent compression of the main artery. The diathermy should not be used in trophic disorders or gangrene. Other non-operative measures which have been employed are the intravenous injection of radium chloride (4), triple typhoid vaccine, typhoid "H" antigen (7), or acetylcholine (70). In typhoid bacilli resistant cases, the injection of 2 per cent sulphur in olive oil intramuscularly has also been recommended (69).

Ligation of the femoral vein has been recommended (44, 71); Morton and Pearse (47) tried it in 6 cases. It improved the circulation, increased skin and muscle temperature, and reduced pain. In view of the fact that Buerger's disease involves the veins as well as the arteries, not much can be expected from this procedure. The same may be said for arteriovenous anastomoses.

In cases with a marked spastic element, various operations designed to abolish sympathetic vasoconstriction have been applied. The simplest of these, periarterial sympathectomy, was successful in a small percentage of cases (9). The vascular nerve supply is segmental. Not much, if any, value can be expected from denervating a segment of artery when this disturbs but slightly the whole arterial tree beyond this segment. To meet this objection, more drastic denervation operations were tried which culminated in the operation of thoraco-lumbar sympathetic ganglionectomy with trunk resection (1, 2, 14, 31). The operation is formidable. It gives good results in predominantly spastic diseases like Raynaud's disease and in early vasospastic scleroderma. It is too heroic an operation to be justified in early cases of Buerger's disease. The cases with frank gangrene do not permit the procrastination which this operation entails. It may be applied, however, to moderately advanced cases of Buerger's disease with a marked spastic element and without gangrene. The immediate results in well selected cases of this group are encouraging, but give no guarantee that the thrombo-angiitic process will not proceed regardless of the operation, or that vasospastic control will not be regained through ineradicable anastomoses from other parts of the sympathetic net or from local assumption of automaticity.

The simpler measures outlined when used to reduce the spastic element and to improve the collateral circulation are of great value in preventing gangrene or at least in increasing the amount of available stump. Applied after operation also, they increase the chances of success of less drastic amputations. The use of these simple measures should be encouraged.

Buerger insists that none of the methods used for determining circulatory intensity determine the lowest level at which an amputation stump will heal; that after the various conservative measures have been employed and amputation becomes imperative, amputation above the knee is indicated in all but very exceptional cases

Where possible, he recommends the Gritti-Stokes. Telford states that when gangrene threatens, the popliteal is almost always involved, and that to amputate lower than the knee is to court disaster. The recommendation of this high arbitrary level has met with growing disapproval. It has to recommend it the fact that re-amputations are avoided and that hospitalization is minimized. Further, Buerger's disease is a progressive lesion and high amputation may anticipate its advance. On the other hand, these re-amputations are avoided at a great deal of needless mutilation. Hospitalization is minimized at the cost of a much greater post-hospital disability. The progress of Buerger's disease is so erratic that no one can say when and where it will stop; it may end with low amputation. Midleg amputations are frequently adequate. This disease occurs in young men of working age who must stave off major disability as long as possible. There is always the prospect of serious involvement of the other leg; therefore, as much as possible of each leg must be spared. Finally, re-amputation, except in cases of spreading infection or spreading gangrene, is of no very great risk in Buerger's disease and is often worth taking a chance on to avoid needless loss of limb.

Each case must be estimated on its own merits, and the lowest level of amputation compatible with healing and function selected. In 1913, McKinley recommended that the diseased vessels be dissected upward until a point is reached where the blood supply appears to be satisfactory, and that amputation be done at that level (8). The method was dropped because the difficulties and complications of the technique were too great to justify it and because it took no account of the collateral compensation. Meleney suggested that if popliteal pulsation were present, amputation could be done below the knee. A later review of his results made him feel less assurance in accepting this one finding as the basis of selection of the amputation level. Burke considered the patency of the femoral artery to be far more important than that of the popliteal. He found popliteal pulsation absent in 50 per cent of successful amputations below the knee. He stated that if a full pulsation of the femorals could be felt to 4 centimeters or more below the inguinal ligament, amputation below the knee could be done even if the popliteal were closed.

As a matter of fact, the selection of an amputation level cannot be based on any one criterion. The problem is too complex to be settled so readily. Allen and Meyerding reviewed 102 cases of amputation in Buerger's disease and suggested some additional factors as of possible significance in selecting this level:

1. The age and general condition of the patient. They found that amputation below the knee would be successful in 80 per cent of the cases when the patient was under 45 and in good condition and there were no extensive local changes. Re-amputation would be necessary in only 20 per cent of cases fulfilling these conditions. They found that in older patients and with extensive local or septic changes, primary amputation above the knee was required.
2. The condition of tissues at the proposed operative site. Considerable muscular and skin atrophy would make the healing possibility unlikely.
3. Lack of economic urge. If the economic situation permitted prolonged treatment, small ulcers and small areas of gangrene often healed spontaneously and function was re-established.

They found that one of the important results of early diagnosis lay in not mistaking the pain and dependent rubor about the toes for a paronychia, and incising it. It is a simple matter to examine all feet routinely for a dorsalis pedis pulsation and for plantar anæmia on elevation. If this shows circulatory deficit in the toes, they should not be incised nor should toe nails be removed without careful study of the circulatory condition of the rest of the limb nor without careful surgical decision and thorough pre-operative and postoperative care. These indiscriminate incisions heal with great difficulty and may lead to spreading gangrene when operative trauma aggravates the vascular deficit and increases the healing load.

Amputation may be required even without any local lesion. With skin intact but with excruciating pain, which cannot be relieved by the medical management outlined, amputation at a proper level is justified.

The selection of an amputation level depends primarily in vascular diseases on the circulatory status of the leg and secondarily on infectious, mechanical, prosthetic, and other factors.

Toe amputation will suffice in Buerger's disease if:

1. The patient is under 45 and in good general condition.
2. The local lesion is limited to a small ulcer or area of dry gangrene involving only one phalanx.
3. The dependent rubor and elevation anæmia is restricted to the toes.
4. An abrupt temperature change level is absent down to the toes.
5. The dorsalis pedis or the posterior tibial pulsation is present.
6. The oscillometer shows a fair total pulsation in the foot.
7. The salt solution or histamine test is satisfactory at the level of the metatarso-phalangeal joints.

If the X-ray reveals the absence of a phalangeal osteomyelitis, and especially if the skin tempera-

ture rise after local nerve block shows a marked spastic element, conservative management should be instituted to reduce the spastic element and encourage collateral circulation development. If healing does not result after full benefit has been obtained from these measures, toe amputation may be done.

If more than toe amputation is necessary, the next available level is midleg. Chopart and Pirogoff amputations are not particularly satisfactory even in feet with normal circulation. Even the Symes amputation is losing favor (68). It is not done at all in women because the prosthesis necessary gives an ankle of abnormal thickness. It was employed for laboring men who had to stand on their feet all day, because of its end bearing qualities. But circulation about the joints is not very rich at best. Bad experiences with sloughing of flaps even in normal legs and improvements in prostheses for the higher amputations have swung surgical judgment to the latter. The maximum length of leg stump practical is 7 or 8 inches. The lower third of the leg, even with normal circulation has not a very good blood supply. A stump longer than 7 or 8 inches invites sloughing and is of no particular mechanical advantage (28, 53).

If the lowest judicious level of leg amputation even in normal legs is 7 or 8 inches below the tibial tubercle, in Buerger's disease sufficiently advanced to require leg amputation, the amputation should be done somewhere above this level. Perfect collateral compensation for vascular obstruction cannot be expected. How high above this level one need go depends on the circulatory status determined. If the popliteal pulse is present, or even with it absent, there are signs of good collateral circulation down to the lower third of the leg, midleg amputations can be done. The oscillometer should register good excursions at the level selected, or else the deficiency in pulsatile collateral flow must be compensated by evidences of an unusually good non-pulsatile flow. Anæmia on elevation and rubor on dependency should not extend above the ankle. The temperature change level should be 10 centimeters below the midleg level. The salt solution or histamine tests must be positive at this level. If the patient be under 45, and the X-rays disclose no extraordinary arteriosclerosis and the area of gangrene and infection does not extend beyond the ankle, midleg amputation may be done. If these conditions are fulfilled and the area of gangrene is small but the infection extends to the lower third of the leg, midleg amputation can still be done if the open technique is used. In proportion as these conditions are not fulfilled, higher amputations must be done, keeping always well above the zone of static vascular deficiency, slightly above the temperature change level, and within the zone of good skin circulation.

Two inches below the tibial tubercle is about the shortest leg stump practical (27). Makers of artificial appliances say that fairly satisfactory service may be obtained even with a 1 inch stump. But the mechanical advantage of this small leverage must be rather slight. Further, circulation close to the knee joint is not particularly good even in normal limbs. The healing power of a Buerger's disease leg which requires amputation at 1 inch below the knee is questionable. In many clinics, the high leg amputations have been replaced by the Gritti-Stokes. The Gritti-Stokes is end bearing if it succeeds. The objection raised to it on the grounds that it elongated the thigh has been answered by the application of an underslung knee joint. The operation requires, however, more manipulation and healing strain than these devascularized tissues can bear. It is end bearing only if the poorly vascularized skin can bear the strain of pressure. It is probable, therefore, that if a leg can stand a Gritti-Stokes, it can stand a lower amputation better.

The Gritti-Stokes may have an occasional indication. If it cannot be done, a supracondylar thigh amputation will serve just as well. The mechanical advantage is as good. The usual type of mechanical joint can be applied. Anatomical bearing shifts pressure from an end which needs all the circulation it has to heal and stay healed, to higher points near the groin, which are much better supplied with blood (55).

Amputation above the knee should be done if full femoral pulsation cannot be obtained to 4 inches below the inguinal ligament; if good oscillometric excursion cannot be obtained just below the knee; if anæmia on elevation and rubor on dependency extend well up the leg; if the temperature change level is just below the knee; if the salt solution or histamine tests are negative to the knee but positive above; if the patient is over 45 or there is extensive gangrene or infection. If these tests show circulatory insufficiency to extend even above the knee, if the patient is still older, the gangrene more extensive, and the infection more severe, amputation at midthigh is indicated. In all these operations, a proximal tourniquet should not be used. Use may be made of the distal tourniquet in order to prevent reflux. Postoperative care must include all measures which are available to develop collaterals and to promote healing.

ARTERIOSCLEROSIS

Arteriosclerotic vascular occlusion is an accompaniment of old age. The patients are in poorer general condition. Cardiac, nephritic, pulmonary, and cerebral complications play a greater and, sometimes, the dominant rôle in the surgical picture. The cellular virility, the lust for life of the tissues locally is reduced. They die easily; they heal poorly. The *blutgefuehl*, the ability of the living tissues to attract vascularization, is diminished (11). The collateral potential is decreased.

The vascular involvement of old age is not patchy as it is in Buerger's disease, but uniform. It strikes not only one or two branches of the vascular tree at a time but the whole tree at once with all its finest twigs. When occlusion becomes manifest, there are no entirely free channels which can open to take up the load. The margin of collateral safety is very small. The process, however, is slow. The duration of symptoms from their onset to the development of serious surgical situations necessitating amputation is very long, except as sudden impulse is given to the occlusive process by infection or thrombosis. Except for these accidents, the limb expectancy with proper care may be 5 or 10 years or longer from onset.

The disease occurs in patients who are usually beyond working age. The economic issue is, therefore, not as pressing as it is in Buerger's disease. Working function in the limb is not as important a part of the amputation decision, and temporizing is better countenanced.

The process is predominately degenerative rather than inflammatory or neuro-circulatory. In the muscular arteries of the extremities, it begins as an increase in the mucinous metachromatic ground substance of the media, for it is the media which carries the burden of functional strain in these vessels. As the mucin increases, the elastic and muscle tissue of the media decrease. Fat deposits; hyalin fibrosis sets in and is soon followed by calcification. Secondarily, the intima is involved, first with fat deposit, then with intimal proliferation. The lipoid is desmoplastic; hyaline fibrosis becomes more and more marked. The fatty placques within the thickened intima break down, calcium is deposited, and finally, ulceration develops. These intimal changes, however, come on only long after the medial changes are well advanced. The patients generally do not have a high blood pressure. Those with high blood pressure usually can keep driving blood through the thickened vessels adequately until one of the hypertension accidents kills them.

A spastic element in the vascular occlusion is sometimes present. It is very variable. Just as in Buerger's disease, it must be estimated and dealt with, but it is usually a small part of the occlusion problem.

Pain is a prominent symptom because of the high grade circulatory insufficiency. It alone may be indication enough for amputation. The blood supply may be worse in a painful leg without gangrene, than when gangrene is actually present. Gangrene is usually precipitated by thrombosis in the diseased vessel or by infection. If the superimposed injury is small, collaterals develop. They develop slowly and poorly in proportion to the patient's age, and not much can be expected from them. It takes months and years for them to develop but enough may develop to avert gangrene for many years even though pulsation be absent. When gangrene does supervene, limited amputation may suffice because of the collaterals even though pulsation be absent. If collaterals do not develop sufficiently, or if the thrombosis is more rapid or extensive or if severe infection supervenes, gangrene results, before collateral circulation can replace the main channel flow and nothing but a high amputation will heal.

When the question of amputation arises, the circulatory status of the limb is determined just as in Buerger's disease. The Matas or Moszkowicz tests are not recommended because of possible injury to diseased vessels. Routine X-rays are taken to determine the amount of arterial calcification, but this gives only a vague estimate of the circulatory intensity. They take no account of the collateral development which, though usually slight, is sufficiently variable so that in some cases at least it will prevent needless loss of considerable limb length.

The history is taken, the severity of symptoms noted, palpation for pulsation, oscillometric excursions, the level and intensity of anæmia on elevation and rubor on dependency, the angle of circulatory sufficiency, the temperature change level, the appearance of the limb when horizontal, the character of the local lesions, and the salt solution or histamine tests are determined. Whatever spastic element is present is evaluated Pre-operative management to reduce the spastic element and encourage collateral development is instituted for whatever benefit may accrue.

Amputation may be withheld for a long time unless there is evidence of spreading infection or a large area of gangrene or intractable pain. Conservative management including active and passive exercises, dry heat, hot baths, abundant fluids and some form of fever therapy, together with proper care of the local lesion along general surgical principles may suffice to heal recalcitrant

wounds or superficial ulcers or well demarcated small areas of gangrene at the tip of a toe, provided there is no gross circulatory deficit and infection is slight. The dorsalis pedis or posterior tibial pulse must be palpable, or if either is not palpable, adequate collateral supply must be shown by warm toes of good color in all positions with a positive histamine test, etc.

Amputation is done when conservative methods fail to stop unbearable pain, fail to heal the ulcer or small area of gangrene, or fail to control slight infection or frank suppuration. It is done when economic exhaustion forces a rapid conclusion of the case. It is done when there is gangrene which includes the whole of one or more toes or more of the foot or leg tissue, or if the gangrene area is small but progressive and non-demarcated, or if there is deep or ascending infection which threatens the patient's life.

Amputation of one or more toes will suffice for the minimal lesions under the conditions described as suitable for conservative management, if conservative management fails. It will suffice in gangrene limited to the toe or in osteomyelitis of a phalanx without gangrene if the dorsalis pedis or posterior tibial pulses are palpable. Or if either is not palpable, evidence of good collateral circulation must be present in the form of freedom from severe pain, a warm foot of good color in all positions with a moderate oscillometric excursion or a good histamine test and a well demarcated lesion.

If these conditions are not fulfilled, a midleg or higher amputation must be done. Midleg amputations will suffice if there is good pulsation in the popliteal artery or if there is good oscillometric excursion at midleg level, if the skin is of good color in all positions and shows no temperature change level down to the ankle, and if the salt solution or histamine tests are positive down to ankle level. It will be seen that a greater margin of collateral safety is required in arteriosclerosis than in Buerger's disease. There must be no rapidly spreading infection and no lymphangitis above the lower third of the leg. The patient should be in good general condition and less than 55 or 60 years of age. In a patient who is blind or who is in such mental or general condition that it is probable he will never walk again, it is safer to do a thigh amputation rather than take chances with a lower amputation in order to save leg length which the patient will never use. It is especially urgent that a midleg rather than a thigh amputation be done when possible if the condition of the other foot is such that subsequent trouble in the latter seems probable.

The best leg length obtainable is 6 to 9 inches below the tibial tubercle; 4 to 6 inches is usually good enough. The fibula is to be cut 1 inch higher unless infection below makes extra operative manipulation inadvisable. The level selected may be raised accordingly as the above conditions are not fulfilled to within an inch or two of the tibial tubercle. In these cases, it is advisable to excise the entire head of the fibula except under circumstances as stated above (Speed).

Above this level, the Gritti-Stokes operation is recommended, but is open to the same objections which were described under Buerger's disease. The operation is more complicated, blood supply to the flaps is not so good, and healing is irregular. Further, the chief reason for which it is chosen, namely, to provide a laborer who has to stand on his feet all day with an end bearing stump, is rarely called for in patients of this age group and general condition. The fact that it is a closed operation automatically excludes it from any case in which amputation is done for infection. If a Gritti-Stokes operation is possible, the mechanical advantage of a supracondylar amputation is just as good and healing is surer.

The elective thigh amputation is done about 3 inches above the knee. It is done when popliteal pulsation is absent, and the skin is not warm and of good color in all positions down to the level of the ankle, when oscillometric excursion in the leg is absent, but is present in the lower thigh or is substituted there by a good histamine or salt solution test, and when the temperature change level is below the knee. It is done if the patient is over 60 years of age or in poor general condition, and in extensive or rapidly spreading infection.

If femoral pulsation is not obtained, if oscillometric excursion in the lower third is weak or absent, if this portion is cold and the histamine test is weak or negative here, or infection has spread to the knee or general sepsis is more severe, a midthigh amputation is done.

It is folly to close an amputation done for sepsis; infection does not stop at the level of skin redness. Far above the hyperæmic zone lymphatics and veins are saturated with organisms and closure of the wound invites disaster. At least half of the postoperative mortality is due to sepsis. Open amputation will not only reduce mortality but will increase length of limb safe to leave.

After recovery, a temporary prosthesis should be fitted as soon as the stump condition permits. Active exercise will even improve the healing power of the stump. This prosthesis is used for 3 to 6 months until the stump has shrunk to its definitive size and an artificial limb can be fitted.

DIABETES

The problem of gangrene in the diabetic cannot be dismissed along with arteriosclerotic gangrene, because only a portion of the diabetic gangrenes are arteriosclerotic. The diabetic is threatened with gangrene from three fronts: arteriosclerotic, infectious, and embolic or thrombotic (42, 43).

Arteriosclerotic gangrene in the diabetic is essentially similar to arteriosclerotic gangrene in the non-diabetic, and is handled in much the same way. It occurs in the old age group. The diabetes itself is probably due to arteriosclerosis in the pancreas and is usually mild and fairly easily controlled. It does not itself court serious sepsis and the gangrene problem remains predominantly that of circulatory deficiency.

The only difference is that once the diabetes is started, it hastens the arteriosclerosis (23, 36). This it does perhaps by virtue of the lipæmia associated with the abnormal metabolism and high fat diets of the disease. We know that as the diabetic factor becomes more prominent, intimal changes in the muscular arteries become more and more prominent in comparison with medial changes. Fat deposition in the internal elastica becomes more and more predominant and medial sclerosis falls behind in the sclerotic picture. The whole process is accelerated and gangrene occurs in the diabetic arteriosclerotic some 10 years earlier than in the non-diabetic arteriosclerotic.

The diabetes itself, though mild, must be reckoned with, and proper dietary and insulin management instituted. A high carbohydrate diet with insulin is preferable to the high fat diet without insulin because the lipæmia of the latter encourages intimal atheromatosis, and it is this factor which not only hastens the vascular occlusion but paralyzes the development of collaterals. At a given age, it is the patient with most medial sclerosis and least intimal changes who has the best collateral development. The diabetes also, though mild, does introduce an added bacterial danger, so that infections must be prevented or treated even more assiduously than in the non-diabetic. The other diabetic hazards of hyperglycæmia or hypoglycæmia, acidosis, and malnutrition must be avoided (5, 33).

In this group of aged diabetic arteriosclerotics, little can be expected from collateral circulation, in most cases. Yet, as in the non-diabetic cases, if the occlusive process is slow enough, considerable collateral development may occasionally occur and permit amputation at a lower level. With the infectious element evaluated, the selection of amputation levels is based on the same criteria as in the non-diabetic arteriosclerotic.

Arteriosclerosis, particularly the intimal type, begins even in young diabetics, provided they have had the diabetes for 5 years or longer. Gangrene occurs in young diabetics, but the chief rôle in the gangrene of young diabetics is played by infection rather than by arteriosclerosis.

In proportion to the severity of the diabetes, the general and local resistance to infection is decreased. Dry gangrenes quickly become infected, superficial infections develop quickly; even gas bacillus infections are particularly prone to develop in diabetics, and the tendency to general septicæmia is marked. The tissues are very sensitive to pressure, heat, or strong antiseptics. This may be due to increased sugar in the tissues, to hyperglycæmia, to ketosis, to the secondary intimal sclerosis, etc. Whatever the cause, the threat of infection in the diabetic is formidable.

When gangrene develops in a diabetic, the younger the patient, the more likely it is that the gangrene is on an infectious basis rather than on an arteriosclerotic. Usually the younger the patient with gangrene, the worse is the diabetes. The worse the diabetes, the greater is the diabetic intimal sclerosis and the greater the inhibition of collateral development. But this is far outweighed by the greater collateral potential of the younger patient, and circulatory embarrassment therefore plays a lesser rôle. On the other hand, though cellular virility is greater in the younger patient, the increased severity of his diabetes more than balances this, and infection is likely to run rampant.

In any case of gangrene in a diabetic, the rôle of the infectious element and the rôle of the circulatory element must be separated and evaluated. The first step in this process as in all types of gangrene is an estimation of the circulatory status of the limb. If the patient is young, the diabetes relatively recent, a history of claudication absent, pain slight and in proportion to the amount of infection, pulsation or good oscillometric excursion present, or if absent, the foot is warm without temperature change level and is of good color in all positions, shows a positive salt solution or histamine test and if infection or gangrene is well localized, the presence of good circulation is established and the case can be handled as a simple infection or as a severe infectious or traumatic gangrene (65). In proportion as these conditions are not fulfilled, circulatory deficiency must be added to the gangrene picture and included in the prognostic and therapeutic decision.

Toe infections, foot infections, small ulcers, and small areas of gangrene should be treated conservatively provided there is adequate direct or

collateral vascular supply. Accurate diabetic management, free incision and drainage, and treatment of the lesion along general surgical principles will take care of the situation. Slight circulatory deficiency can be corrected by the measures instituted under the minimal lesions described in arteriosclerotic gangrene (29).

If good circulation is established, toe amputation may be done for osteomyelitis of a phalanx or to improve drainage of infection in the deep fascial planes of the foot, or for ulcers or small areas of gangrene which remain unhealed after prolonged conservative management. The wound should be left open in all amputations done for infection, in all cases in which the dorsalis pedis did not pulsate, and in all cases of infectious gangrene with or without dorsalis pedis pulsation. Only in direct traumatic gangrenes without infection or in osteomyelitis which is well localized and carries no doubt of circulatory sufficiency can the wound be closed loosely.

Major amputation must be done if the diabetes can no longer be controlled by diet and insulin; if there are signs of a rapidly spreading infection or gangrene; or if there is a local uncontrollable violent infection with signs of septicæmia or severe toxæmia. In these diabetics, the indication for amputation is primarily infectious, but the severity of the infection depends partly on the circulatory status and the level of amputation chosen depends on both.

It is these situations in particular which call for the most careful choice of amputation level. Reamputations are at least five times as dangerous in diabetics as in simple arteriosclerotics. Reamputations add 15 (Eliason) to 35 per cent (McMahon) to the operative mortality in diabetic gangrene. A gangrenous diabetic extremity must be amputated only once and that at a level which will furnish sufficient blood supply and insure control of the infection. No temporizing is permitted. The patient is prepared as for potential diabetic coma, and decisive amputation done at once (24, 50, 59).

On the other hand, it is just this group of young diabetics with good circulation who suffer needlessly high amputations and are left needlessly crippled because the gangrene they present is treated in the same way as the senile arteriosclerotic type. It is not necessary to go always above the knee. In this group with a good direct or collateral vascular supply, the amputation can be done on the infectious indication only, and thereby limb length saved.

Midleg amputation can be done in patients under 45 or 50 (reckoning that arteriosclerosis is hastened by 10 years in diabetics), if the patient is in good general condition; if the infection is restricted to below the ankle and adequate circulation established. By adequate circulation is meant popliteal pulsation or good oscillometric excursion in the middle third of the leg with good temperature and color down to the level of the ankle, and a positive histamine reaction as low at least as the amputation level. With the same degree of infection, the poorer the circulatory status, the higher the amputation must be.

The Gritti-Stokes is not recommended because this situation in particular does not admit prolonged operative maneuver. Longer and better healing stumps will be left with less complex operations (Maes, 39).

Amputation is done above the knee in patients over 45 or 50, or who are in poor condition, or when gangrene involves the entire foot, when infection spreads above the lower third of the leg, or even with less severe infection when circulation cannot be established below the knee. For all these amputations for infection, the open operation will permit greater stump length; will insure better control of infection and eventual healing.

The third type of gangrene in the diabetic, that due to an embolic or thrombotic accident, depends entirely upon the previous circulatory and infectious condition of the limb. Prognosis and treatment depend on these latter factors in addition to the size of the embolus or the thrombus and the development of secondary thrombosis. The diabetes itself is only a complication which makes circulatory deficiency more likely and secondary infection more virulent. Except with very small emboli or thrombi, collaterals have no time to develop. Young patients with good previous circulation can weather a much more severe acute occlusion than older patients with previous circulatory damage. Embolectomy could then be done were the patient seen early enough, or could even be done later to improve circulation after the original onslaught had subsided. Myocotic emboli are more poorly borne than the bland. In older individuals with poorer previous circulation or with larger emboli or rapid secondary thrombosis, the prognosis is bad. Amputation must eventually be done at the level of circulatory insufficiency determined by the tests described.

SUMMARY AND CONCLUSIONS

An attempt has been made to analyze the amputation criteria invoked in cases of circulatory disturbances of the lower extremities on the basis of the pathogenesis of the underlying conditions.

The primary element in the amputation decision is an estimate of the circulatory status of the limb. The importance of pre-operative and post-operative management to encourage collateral development is emphasized.

Amputation need not always be done at or above the knee in Buerger's disease. It is done at the lowest level compatible with the assurance of healing given by the circulatory tests.

In arteriosclerosis also, careful circulatory study can save limb length. Not all diabetic gangrenes are to be handled alike. One group is essentially arteriosclerotic, the other group is essentially infectious. Diabetes is common to both only as a complication, and the proper amputation levels are widely different.

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TORSION OF THE FIBROMATOUS UTERUS[1]

A Surgical Emergency

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TORSION of an abdominal viscus or tumor, with the consequent interference with the blood supply, constitutes a serious surgical emergency. Torsion of any of the abdominal organs (except the liver) may occur, and twists of a pedunculated tumor, usually an ovarian cyst or fibroid, are relatively common. Rotation of a fibroid uterus, on the other hand, is but rarely encountered, as might be expected when one considers the stability of the normal organ, supported as it is by the broad and the round ligaments which, while permitting fairly free movement in an anterior and a posterior direction, furnish considerable resistance to any lateral torsion. When, however, the uterus is enlarged, and rising out of the pelvis becomes an abdominal viscus, the cervical segment is elongated, the ligaments are stretched, and the chance of a torsion becomes greater. Cases of torsion of a pregnant uterus have been reported; but while they have a number of points in common with torsion of a fibroid uterus, they will not be considered in this paper; the reader is referred to articles by Robinson and by Feiner and Kaldor, the latter of whom were able to collect 11 such cases. Tumors of the adnexa may also cause torsion of the uterus, but these again are not discussed in this report; readers are referred to Girod, who, in reporting 87 cases of torsion of the uterus produced by tumors, considered that the rotation was produced by tumors of the adnexa in 33 cases[2] and by fibroids in 54.

In looking through the literature we have been able to collect only 8 cases of torsion of a fibroid uterus reported from the United States; many more cases, however, have been reported from other countries and a fairly extensive European literature on the subject exists. A brief review of this material will be given later in this paper. The following case is reported because it represents an interesting, and somewhat rare, example of emergency surgery for acute abdominal pathology.

Case No. 9127, Mary Imogene Bassett hospital. On August 13, 1933, E.B., a 62 year old married housewife, a native of New York State, was admitted to the hospital. She complained of abdominal pain of 4 days' duration and abdominal tumor of 2 years' duration. The family history was not important. The more pertinent points only of the past history are presented:

Patient has been married for about 43 years; there were 2 full term pregnancies, 42 and 20 years ago respectively. The first delivery was instrumental and she suffered severe lacerations of the perineum. For a number of years the patient has been troubled by frequency of urination and burning. Menses began at the age of 12 and were always essentially normal; menopause occurred 12 years ago. She has suffered considerably from leucorrhœa; for the past few years the discharge, which was previously whitish in color, has become dark brown.

The patient has had no recent neurological symptoms, except that at times she has been troubled by numbness and tingling of her fingers. In 1907, 26 years ago, she had a perineal repair and suspension of the uterus. About 5 or 6 months ago, on two occasions within a period of a few days, there was a small amount of vaginal bleeding, amounting to a few teaspoonfuls of blood on each occasion. Two years ago the patient noticed a "small tumor" in the lower left part of the abdomen; since that time the abdomen has increased in size. For the first year there were practically no symptoms; about a year ago she noticed a heavy, dragging sensation in the lower abdomen, with some backache; at times she has had attacks of acute lower abdominal pain. During the past 2 months her abdomen has rapidly increased in size; she has felt increasing weakness, and has begun to suffer from shortness of breath, palpitation of the heart, and frequent gaseous eructations from the stomach. She has lost a good deal of weight, her best weight having been 200 pounds, her weight on admission 170 pounds. In spite of her symptoms, however, she has been able to carry on an active life and to do her own housework.

Four days before admission the patient noticed a dull, aching sensation in her lower abdomen and left thigh, and a few hours later she was taken with pains, sharp and knife-like in character, across her lower abdomen, particularly on the left side. The pain persisted throughout the following day and her abdomen became exquisitely tender; she had considerable dyspnœa and felt dizzy and faint. For the past 2 days she has been under the care of her physician, who has given her a considerable amount of morphine because of the severity of her pain. She has vomited on a number of occasions and has felt nauseated most of the time; any movements, such as turning over in bed, have greatly increased the abdominal pain, especially when she has been lying on her right side. The bowels have moved several times since the onset of the attack of pain; the patient has had urinary frequency, which she has suffered from for a number of years.

Physical examination revealed the following: Patient was an elderly woman with marked pallor of skin and mucous membranes; there was some cyanosis of her nail-beds. She appeared to be acutely ill; respirations were somewhat rapid and grunting; pulse rapid, thready and barely palpable. She lay on her left side and cried out in pain if any attempt was made to move her; she belched gas frequently.

[2] These he listed as follows: cyst of left ovary, 15; cyst of right ovary, 6; cyst of ovary, side not designated, 6; tumor of ovary, 3; and parovarian cyst, 3.

[1] From the Surgical Service of the Mary Imogene Bassett Hospital

Examination of the head was negative. Heart and lungs were essentially negative except for tachycardia. The abdomen was markedly distended by a tumor mass as large as a full term pregnant uterus, and apparently slightly more prominent on the left than on the right side. Dullness was present over the abdomen, except in the right flank and epigastrium, where there were areas of tympany. No fluid wave was noted. The tumor mass was apparently smooth; no nodules were made out. Marked tenderness, even on light pressure, was noted over the whole abdomen. Pelvic examination was not very satisfactory; the cervix was small and high in the vagina; no tumor mass filled the pelvis; the body of uterus could not be identified.

On admission the patient's temperature was 102 degrees, pulse 130, respirations 24.

Pre-operative laboratory findings: Red blood cells, 2,400,000; white blood cells, 21,500; hæmoglobin, 45 per cent; polymorphonuclears, 88 per cent; eosinophiles, 1; basophiles, 0; large lymphocytes, 2; small lymphocytes, 8; mononuclears 1; platelets diminished; moderate anisocytosis, poikilocytosis and achromia; non-protein nitrogen, 51 milligrams. Urine: clear amber; specific gravity, 1022; reaction, acid; albumin, heavy trace; acetone, negative; sugar, negative; occasional white blood cell; rare red blood cell.

Treatment. The exact pathology responsible for the acute attack was not clear; in spite of the indications of a strangulated tumor, the fact that the patient had been losing weight and strength for a year, with marked anæmia, raised the question of abdominal neoplasm with some added complication. An exploratory operation seemed to offer the only help, but it was felt that unless her condition could be somewhat improved she would not survive even the simplest operative procedures.

On the night of admission the patient was given an intravenous infusion of 1000 cubic centimeters of 10 per cent glucose, which brought some slight improvement. On the next day, however, her condition was extremely critical, the pulse was barely palpable at the wrist and she was mentally stuporous and confused. Following transfusion of 500 cubic centimeters of whole blood, her condition was somewhat improved; a small stomach tube was passed and a considerable amount of gas and small amount of fluid drawn off, giving her much relief. She was given another intravenous infusion of 10 per cent glucose. On the following morning her condition seemed to be definitely better, and it was felt that we could proceed with an exploratory operation under novocain as the anæsthetic.

Operation. Under novocain anæsthesia a small exploratory incision was made at about the middle of the abdomen through the left rectus muscle. The tumor that presented in the wound after incising the peritoneum did not appear to be malignant; it was smooth, non-adherent, soft, and elastic on palpation. Since the patient's condition was so precarious it seemed desirable, if possible, to aspirate the enormous tumor to facilitate its delivery; a hollow needle was accordingly introduced, but the tumor was found to be solid. The incision was then greatly enlarged, both upward and downward, following which it was possible to deliver the whole tumor. The picture presented was striking: the main mass of the tumor consisted of a large fibroid uterus which had undergone rotation, apparently making a complete turn of 360 degrees, clockwise, at the cervical segment; the broad ligaments, tubes, and ovaries were black and gangrenous in appearance, the broad ligaments distended with extravasated dark colored blood clots.

After the torsion was reduced, a supravaginal hysterectomy was carried out. The uterine arteries and vessels of the broad ligaments were transfixed and ligated, and the uterus amputated. The cervical stump was closed over with interrupted silk sutures; the abdominal wound was then closed in layers. Silk sutures were used throughout the operation. The patient's general condition improved definitely as soon as the abdominal tumor had been delivered.

Postoperative progress. The patient's condition on the day after the operation was satisfactory; temperature 100.2 degrees, pulse 98. She had considerable gaseous distention (as was to be expected, since the intestines were considerably distended at the time of operation), which yielded to simple measures: the stomach was kept empty by means of a small stomach tube passed through the nares, liberal doses of morphine were given, and flaxseed poultices and rectal tubes employed. The patient was given intravenous infusions of glucose and saline.

For the first few days the patient was mentally "flighty," a little confused at times, talking somewhat irrationally. Her convalescence on the whole, however, was smooth and satisfactory. The abdominal wound healed by first intention. For some time she ran slight evening elevation of temperature (about 101 degrees rectal), for which no adequate explanation was ever found; possibly it was related to some chronic infection of her urinary tract, or there may have been some phlebitis of the pelvic veins. Her anæmia improved markedly after the administration of iron and liver extract. The patient was discharged in excellent condition on October 5.

Pathological report. The report of the gross examination of the specimen removed at operation is as follows:

"Specimen consists of a large tumor weighing 13½ pounds and measuring 24 by 21 by 21 centimeters (see Fig. 1). The surface is smooth and dark-purplish red in color, marked by dilated superficial veins. At several points it is discolored and dark bluish-black, apparently from superficial subserosal necrosis. Attached to either side near the pedicle are very large broad ligaments filled with blood; on neither side can the ovary be positively identified. The raw area where the tumor was removed from the body measures approximately 13 by 6 centimeters and is roughly oval in shape.

"On section, the upper four-fifths of the tumor is composed of firm tissue arranged in irregular masses varying in size from 1 to 10 centimeters in diameter (see Fig. 2). These islands of tissue have a fibrous-like structure for the most part and they stand up above the intervening interstices. Toward the cervical end of the mass the tissue is of different structure, suggesting normal uterine muscle extensively infiltrated with blood."

Microscopic examination showed the typical picture of fibromyoma of the uterus.

HISTORICAL SURVEY

Although Times (1861) is considered the first to have reported an observation of axial rotation of the uterus, the exact pathological condition in his case is not clear from the data presented.

In 1863 a case of torsion of a myomatous uterus was described by Virchow. In this instance the twist was found at autopsy in a 63 year old woman who had died of pneumonia.

Following Virchow's case many others were reported, especially in the German literature. Outstanding studies have been made by Schultze, in articles appearing in 1898 and 1906; by Girod, who gave a complete résumé in 1908 of 54 cases (including those reported by Schultze); by

Piquand and Lemeland, who, in 1909, discussed not only cases of torsion of the fibromatous uterus itself but also twists of pedunculated fibroids; by Hitzanidés, who added 8 new cases to the collection in 1926; and by Peightal, who, in 1929, collected 47 cases that had appeared in the literature since Hitzanidés' article, and added 1 of his own. Peightal considered that although it was impossible to give exact figures, since different authors included different types of cases[1], at least 133 cases had been reported up to that time. Since Peightal's article in 1929, 6 have been reported in the literature and are here briefly summarized.

SUMMARY OF CASES REPORTED SINCE 1929

1. Reported by Cotte. Patient, a married woman of 38 years, was waked from sleep 24 hours before admission by an acute attack of abdominal pain; no nausea or vomiting. A tender abdominal mass was palpable.

Operation revealed multiple myomata; the uterus was twisted from left to right 180 degrees. Myomectomy was done and the uterus returned to position; result, cure.

2. Reported by Santy. Patient, a married woman of 27 years, suffered an acute attack of pain 20 days before admission; she had had a similar attack, lasting a few hours, a year before. Apparently she had a large hypogastric tumor.

Operation revealed a purple, gangrenous tumor adherent to the fundus of the uterus, which was also gangrenous and was twisted on the isthmus. Subtotal hysterectomy was done, resulting in cure.

3. Reported by Courty (6). Patient, a woman of 63 years, was seized 14 hours before admission by sudden, severe attack of pain and shock with vomiting; she was *in extremis* when admitted. A tender abdominal mass, the size of a head, could be felt. Patient was known to have had an abdominal tumor 20 years before admission, with minor abdominal crises since then.

Operation revealed a pelvis full of serohæmorrhagic fluid; large tumor on the fundus. Direction of twist was not indicated; weight 3,800 grams. Pneumonia set in on the sixth day after operation and patient died.

(Courty also discusses 2 cases, one simulating intestinal obstruction and the other characterized by repeated minor attacks, reported by other men.)

4. Reported by Courty (7). Patient, a married woman of 45 years, was taken with violent abdominal pain, nausea, and vomiting. Examination showed a large abdominal tumor, apparently of the uterus.

Operation revealed a left to right torsion of uterus at the isthmus; fibroid occupied the whole body of uterus and was red violet in color. Subtotal hysterectomy was done and patient recovered.

5. Reported by Werneck. Patient, an unmarried woman of 38 years, entered the hospital with a hard, painful tumor. The pain radiated from the lower abdomen to the sacral region of the back, and had been increasing in severity. The menstrual periods had been normal until 11 months ago, when they became irregular; the last period was a month before admission.

Examination revealed that the abdomen was distended by a hard nodular tumor extending above the umbilicus. The hymen was intact. Rectal examination was painful; the tumor seemed slightly movable. A diagnosis of uterine myoma was made.

At operation a tumor arising in the pelvis was found, its upper border attached to the ileojejunal portion of the intestine. After freeing the adhesions, the tumor was delivered; it was found to be a fibroid uterus, twisted at the isthmus from left to right; the ovaries were located lying close to the pedicle of the twist. Subtotal hysterectomy and bilateral salpingectomy were carried out.

The tumor was dark red in appearance, and about the size of a 6 months' pregnancy. There were numerous fibroid nodules over the surface. Longitudinal section showed necrosis of the entire tumor and uterus, due to the twist at the isthmus of the uterus.

Convalescence was uneventful.

6. Reported by Battaglioli. Patient was a woman of 39 years, who had been married for 16 years; she had never been pregnant. After amenorrhœa of 50 days' duration, she had a sudden pain in the left side of the abdomen and a bloody vaginal discharge which lasted for a week. After the patient had recovered from the acute attack she was seen by Dr. Battaglioli, who found a hard, painful swelling, about the size of the head of a full-term fetus, in the left lower quadrant of the abdomen. Pelvic examination showed the same mass. Diagnosis: fibroma with twisted pedicle.

Operation revealed an extrapelvic tumor, with omental adhesions, attached to the left cornu of the uterus by a pedicle which was twisted from right to left through 270 degrees; the body of the uterus had undergone similar torsion. The adhesions were severed and a hysterectomy carried out.

SUMMARY OF CASES REPORTED IN THE UNITED STATES

Eight cases were found in the literature, as noted before, and are summarized below. The first case was reported by Homans in 1892.

1. Reported by Homans. Patient, an unmarried woman of 58 years, suffered a sudden attack of severe pain with vomiting. She was known to have had fibroid tumor of uterus for 16 years. On examination, the abdomen was found to be very tender; a hard, round tumor extended above the umbilicus.

Operation was advised but refused; patient died on thirty-ninth day of illness.

Autopsy showed fibropurulent peritonitis. Lower abdomen was filled with smooth, rounded growth extending above umbilicus and covered with adherent omentum. The tumor was dark outside, purple inside; to it was attached a smaller mass, apparently body of uterus. "The twist was very tight, resembling a rope, and in it were contained, in addition to the flattened body of the uterus, both broad ligaments with their contents. Both ovaries were more or less cut off from their blood supply." The torsion was from left to right, "one and a half times"; weight of tumor about 6 pounds.

2. Reported by Goffe. Patient was a single woman, 45 years of age, who had been treated for the past 18 months for "intestinal indigestion."

Operation performed was a supravaginal hysterectomy; patient recovered.

Specimen removed at operation showed an interstitial fibroid, arising from the posterior wall of the uterus, twisted from left to right through 180 degrees; the entire tumor with attached cyst, reached upward to the liver;

[1] Some authors, for example, include torsion of the uterus during pregnancy and some do not.

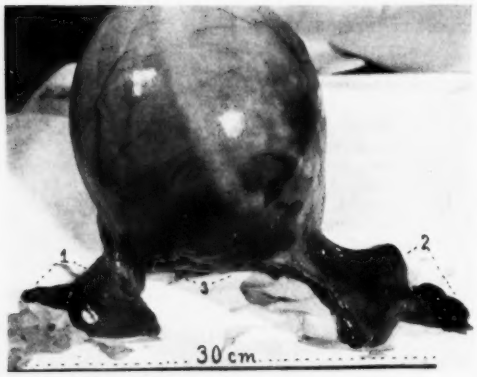


Fig. 1. Photograph of the specimen removed at operation. Weight, 6.1 kilograms (13½ pounds). Note the relatively symmetrical development of the tumor. *1* and *2* indicate the left and right broad ligaments, tubes and ovaries, heavily infiltrated with extravasated dark colored blood; *3* shows the point of amputation.

the ascending colon was somewhat obstructed, with resultant dilatation of the cæcum.

3. Reported by Mundé (18). Patient was a girl of 19 years, with a tumor, the size of a 6 months' pregnant uterus.

Operation revealed a fibrocystic growth of the uterus springing from the left horn by a pedicle 3 inches in diameter; the cyst was black and partly gangrenous; the uterus was twisted so that tumor lay on its right side.

The tumor was amputated; recovery was uneventful.

4. Reported by Mundé (19). At a meeting of the Woman's Hospital Society, Dr. Mundé reported a case of myoma uteri with torsion of the uterus and tuberculosis of one tube.

5. Reported by Foerster at a meeting of the New York Obstetrical Society. Dr. Foerster presented a pathological specimen showing uterus and myoma which had turned "to an angle of fully 90 degrees."

6. Reported by Erdmann. Patient, a widow of 50 years, had an acute attack of pain of 2½ days' duration; signs of collapse; temperature, 102 degrees, pulse, 126; distention. and sense of fluctuation over the left side of the abdomen. She was known to have had 2 previous attacks of severe abdominal pain; menopause occurred 5 years before admission. Her condition was regarded as due to a large uterine fibroid with twisted pedicle, or ovarian cyst.

At operation torsion of the uterus was found; the pedicle, which consisted of an elongated cervix, was twisted two and a half times. Total hysterectomy resulted in uneventful recovery.

7. Reported by Daland. Patient, a married woman of 42 years, entered the hospital with pain in the right lower and middle portion of the abdomen. Two years before she had noticed a freely movable lump in the right lower quadrant of the abdomen; 11 and 5 months ago she had suffered attacks similar to the present. Temperature, 100 degrees, pulse, 120, respiration, 22; white blood cells, 17,800. A tender mass, the size of a baby's head, could be palpated in the lower abdomen.

Operation revealed blood, with clots, in the peritoneal cavity; the uterus was as large as that of a 6 months' pregnancy, rotated 180 degrees; asymmetrical myomata. Subtotal hysterectomy resulted in recovery.

8. Reported by Peightal. Patient, a married woman o 58 years, entered the hospital with pain, nausea, an vomiting of 24 hours' duration; temperature, 100 degree pulse, 112, respiration, 28; white blood cells, 18,000, polymor phonuclears, 82 per cent. She had had two or three simila attacks during past 2 years. Physical examination showe abdominal distention, tenderness, and muscle spasm lower abdominal tumor extended 3 inches above umbilicus During 24 hours following admission, pain became less an general condition better; white blood cells rose to 24,000 polymorphonuclears to 90 per cent; temperature to 101. degrees.

Operation revealed a liter of bloody fluid in the peritonea cavity; fibroid growing from the fundus, torsion in th region of the isthmus, 180 degrees left to right; bluish black appearance of early gangrene; adnexa elongated, swollen and cyanotic. The torsion was easily reduced. Tota hysterectomy was done and a tumor weighing 2,600 grams removed. Patient recovered.

PATHOLOGY

The tumor responsible for torsion of a uterus is usually large, commonly (according to Peightal) weighing over 2 kilograms. In the literature, the size is often compared to that of an infant's or adult's head (13). Extremely large tumors, weighing 30 pounds and 11 kilograms respectively, have been reported by Piccinini[1] and by Faure.

The fibroids may be single or multiple, sessile or pedunculated (16). Hitzanidés believes that when a pedunculated tumor is responsible for the torsion, the pedicle is usually attached near the midline of the fundus[2]; and that sessile or interstitial tumors are usually situated on one side of the uterus, producing an asymmetrical tumor. (In this connection it is interesting to note that the tumor reported in this article developed symmetrically, as shown in Figure 1, by the position of the right and left tubes.) The fibroid may arise from an atrophic or hypoplastic uterus, as occurred in cases reported by Bland-Sutton and Bucura. Degenerative changes in the tumor may take place before the twist occurs, as was true in a case reported by Auvray in which the tumor had become calcified prior to producing the twist.

The changes that take place in the uterus and fibroid following torsion depend upon the extent of the interference with the circulation. Due to the rather loose relation of the uterine arteries to the uterus at the isthmus, where the twist usually occurs, and also to the collateral circulation from the ovarian arteries, the circulation is rarely completely interrupted; degenerative changes, however, do take place, varying from œdema, infiltration, and congestion, to necrosis but extensive necrotic changes seldom occur As is usual in strangulations of any organ, the

[1] The woman was 4 months' pregnant.
[2] This, however, was not the location in Sohn's case.

venous return is the first to suffer. Hæmorrhagic infiltration under the peritoneal coat may give a dark red or violet-purple appearance to the tumor (20). Bloody fluid may be found in the peritoneal cavity (8).

In the case reported in this paper, in spite of the severe twist and the long duration, the main body of the tumor showed surprisingly little evidence of disturbance to its circulation, the principal damage occurring in the broad ligaments, tubes, and ovaries, which were heavily infiltrated with dark colored coagulated blood. As will be noted from Figure 2, the hæmorrhage also extended upward from the broad ligaments under the peritoneal coat of the uterus. The ovarian tissue had degenerated so that it could not be identified in the histological sections taken from the region of the ovary. Gordon-Watson and Shaw record that in their case, also, the fallopian tubes and ovaries were deeply congested and showed early necrotic changes. The extent to which the adnexa may suffer in the more severe torsions of the uterus is clearly illustrated in the accompanying cuts (Figs. 1 and 2).

Polak and Mazzola have studied experimentally the effects of torsion of the uterus on the vessels of the parametrium and contiguous tissues, and found that displacement of the uterus caused an increase in the size of the organ and in the size and number of the vessels. Presumably these experimental torsions are comparable only to the chronic clinical types discussed later.

The bladder (according to Peightal) at times shows compression and œdema of its walls. An intestinal loop may become involved in the rotation, resulting in intestinal obstruction (6, 14); the intestines may also show considerable gaseous distention (as occurred in the case here reported), due to functional disturbances of motility. If the torsion persists for any appreciable length of time before being reduced, adhesions to all surrounding structures may take place (20).

The torsion. The torsion usually takes place at the isthmus of the uterus. As a rule this structure is gradually thinned and stretched as the tumor increases in size; rarely, the whole uterus is elongated and involved in the twist (12). The direction of the twist is usually from left to right: that is, clockwise (15, 16); instances have been reported, however, in which the twist was counterclockwise (9). The degree of rotation is usually 180 degrees, although it may be only 90 degrees. Among Girod's cases, of the 57 where the degree of rotation is stated, 58 per cent were twisted 180 degrees; 7 cases were reported as

Fig. 2. A longitudinal section through the tumor mass. *1* indicates the right broad ligament, tube, and ovary; *2*, an old blood clot extending upward underneath the peritoneal covering of the uterus.

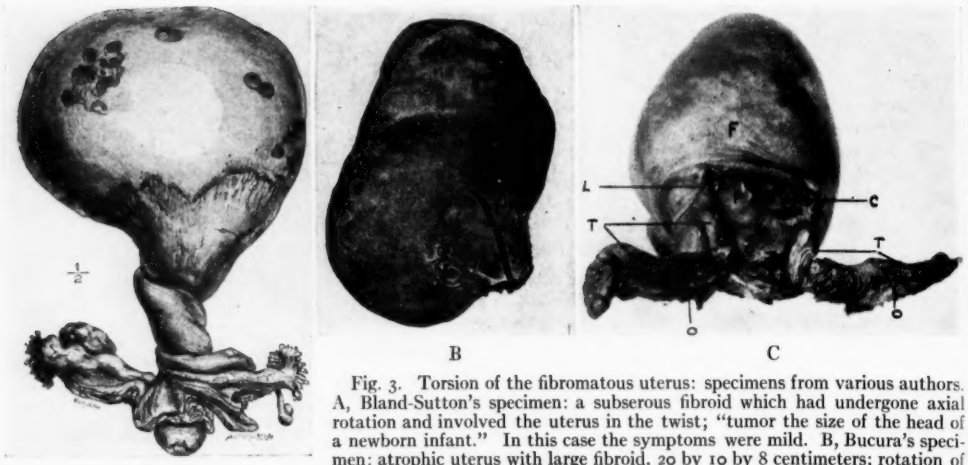
360 degrees (which is the degree of torsion in the case here reported); a twist of 450 degrees has been recorded by Gordon-Watson and Shaw.

ETIOLOGY

There has been considerable speculation as to the cause of torsion of the uterus. The condition is usually found in women over 40 years old (which of course fits in with the prevalence of large fibroids among this age group) and occurs most often in old women (30). An occasional instance has been reported in young women. Mundé (18) reports a case in a girl of 19. In this case the tumor responsible for the torsion was said to be about the size of a 6 months' pregnant uterus.

Usually before a rotation occurs the growth of the tumor has produced a thinning and stretching out of the isthmus, so that when, eventually, the uterus becomes an abdominal organ the isthmus constitutes a pedicle and the immediate mechanism of torsion is that of torsion of any pedunculated tumor, as for example an ovarian cyst. It is probable that movements of the body (such as bending down, turning over in bed, etc.) are important in initiating the twist; asymmetry in the growth of the tumor may be an additional factor; the filling and emptying of the bladder and sigmoid have been suggested (20, 30) but it is difficult to see how this movement could exert a force sufficient to twist a large, heavy tumor.

Difficult as it is to explain the occurrence of one twist, it is even harder to say why multiple twists take place. In the case here reported, in which the rotation was through a circle of 360 degrees, the patient had had attacks of abdominal



A B C

Fig. 3. Torsion of the fibromatous uterus: specimens from various authors. A, Bland-Sutton's specimen: a subserous fibroid which had undergone axial rotation and involved the uterus in the twist; "tumor the size of the head of a newborn infant." In this case the symptoms were mild. B, Bucura's specimen: atrophic uterus with large fibroid, 20 by 10 by 8 centimeters; rotation of 90 degrees found at operation. C, Peightal's specimen: weight 2.6 kilograms; sessile fibroid, developed from top of fundus. *C*, amputated cervix; *F*, fibroid; *L*, round ligament; *T*, tubes; *O*, ovaries.

pain in the past, and it is possible that the first twist of the tumor took place a number of weeks before admission to the hospital, another occurring at the onset of the attack which brought her into the hospital.

The question as to why the rotation occurs to the right more frequently than to the left has also been a subject of considerable speculation; but no adequate explanation has been offered. It has been suggested (15) that since a pregnant uterus becomes somewhat dextrorotated as it increases in size, the same change may occur in the growing tumor.

CLINICAL PICTURE

The cases fall into two clinical groups: one giving an acute, fulminating picture similar to that encountered in twists of an ovarian cyst or pedunculated fibroid, the second presenting mild symptoms which sometimes continue over a period of years.

In the group of acute cases the attack is apt to come on suddenly, with excruciating pain, and is often accompanied by nausea, vomiting, and varying degrees of collapse. Physical examination discloses an abdominal tumor, tenderness and muscle spasm; the tumor may be nodular, suggesting a fibroid, rather than an ovarian cyst. Vaginal examination may or may not be helpful, depending somewhat on the size and location of the tumor. In the case here reported, no mass could be palpated in the pelvis, because the tumor was entirely abdominal; the cervix could be palpated high in the vagina, as is frequently noted in these cases. There is ordinarily some elevation of the temperature and pulse rate, and a leucocytosis is usually present. This syndrome usually points to a strangulation of a tumor; and because of the frequency of twisted ovarian cyst, that is often the diagnosis made.

The second clinical syndrome is that of the chronic or subacute case in which the twist is not sufficient to produce extensive vascular changes causing severe symptoms. There may be a history of attacks of low abdominal pain over a period of several years, and of irregular menses; discomfort and frequency of micturition were important symptoms in a case of the chronic type reported by Bland-Sutton. In this group of cases it has been stated that the fact that a uterine sound or catheter cannot be passed into the uterine cavity is an important diagnostic point. The subacute or chronic symptoms may be followed by an acute attack which may, as suggested in this case report, be occasioned by a second twist.

TREATMENT

In all cases of the acute group and probably in most of the chronic variety, laparotomy is indicated. As has already been pointed out, the severity of the symptoms in the acute group indicates interference with the circulation; and it is desirable that operation be carried out before secondary degenerative changes occur. In case the patient is in collapse, appropriate treatment should, of course, be carried out before

he is subjected to operation. In the case here presented, the attack had started 4 or 5 days before the patient entered the hospital, and her condition was extremely precarious; it was felt that the improvement of her general condition by transfusion and by intravenous infusions of 10 per cent glucose prior to operation, even though it involved further delay, contributed to the favorable outcome.

The type of operation selected must, of course, depend upon the pathology found. Supravaginal hysterectomy is usually indicated, although at times a more conservative procedure such as myomectomy is the operation of choice.

SUMMARY

1. A case is reported of torsion of a fibromatous uterus occurring in a woman 62 years of age, and producing acute symptoms and collapse. Pre-operative treatment consisted of transfusion and intravenous glucose infusions; operation was supravaginal hysterectomy under local anæsthesia; the patient recovered.

2. Approximately 140 cases have been reported in the literature, 8 being from the United States. The cases from the United States are abstracted, together with 6 cases from other countries which have appeared in the literature since Peightal's article in 1929.

3. In considering the pathology it is noted that the tumor responsible for the twist is usually large, and may be single or multiple, sessile, or pedunculated. The changes taking place in the uterus and fibroid depend upon the extent to which the circulation is cut off, and vary from œdema and congestion to necrosis.

The torsion usually takes place at the isthmus; the twist is commonly from left to right, and may be through as few as 90 degrees or as many as 450.

4. In regard to the etiology, there are a number of factors that are not clear; certain facts, however, may be noted. Before the rotation occurs, there is usually a thinning and stretching of the isthmus as the tumor increases in size, so that this structure forms a pedicle which may readily be twisted. Asymmetry in the growth of the tumor may be a factor in the torsion; movements of the body may be important in initiating the twist.

5. The cases fall into two clinical groups: one giving an acute, fulminating picture similar to that encountered in twists of an ovarian cyst or pedunculated fibroid, the second presenting mild symptoms which sometimes continue over a period of years.

6. Prompt operative treatment is usually indicated, with appropriate pre-operative treatment to combat shock, if this complication is present.

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CERVICAL NEUROFIBROMA

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TWO cases of cervical neurofibroma, recently encountered, have renewed our interest in the subject and have prompted this review and study of 17 such cases in which operation was performed at The Mayo Clinic between July, 1924, and January 1, 1934. This group of cases is exclusive of those neurofibromata arising from the brachial plexus or the spinal cord. Writing of this paper is not undertaken with the expectation of presenting anything new; rather, it is to re-emphasize points in connection with neurofibroma (particularly of the neck) which should be familiar to physicians. It is of importance to both physician and patient that this tumor be correctly understood.

ETIOLOGY

The etiology of neurofibroma is not definitely known, although in many instances there is to be found a most interesting familial background. Gardner and Frazier have reported a family of five generations, with 217 members, in which bilateral deafness was transmitted as a mendelian dominant character. Thirty-eight members were affected, 2 of whom came to necropsy and were proved to have bilateral acoustic neurofibromata. Fleming and Marvin have reported 3 cases of multiple tumors of peripheral nerves occurring in the members of one family, although in 2 instances the tumors developed following trauma. There are others, as Gatch and Ritchey, who, although inclined to feel that heredity plays an important part in the formation of neurofibroma, do not dismiss lightly the factor of trauma. Warthin, Blodgett, Brough, and Lehman expressed the belief that neurofibromata are congenital in origin, and are the result of some malformation of the ectoderm. In respect to etiology in the 17 cases of neurofibroma of the neck to be considered here, 8 patients gave histories of malignant disease in their immediate families. The percentage of error, however, may be rather great, for we are unaware how many of these relatives gave microscopic proof of the malignancy; nevertheless, it does seem significant that so many patients in this series apparently had blood relatives suffering from carcinoma or sarcoma.

In Case 17 there was a definite history of trauma preceding discovery of the tumor, but the interval between injury and development of the tumor was not stated, and we feel that this is merely a coincidence.

PATHOLOGY

Grossly, neurofibromata are rounded or spindle shaped tumors, with smooth surfaces and of rather firm consistency. As a rule, they are fairly well encapsulated, but this is by no means constant. The cut surface is yellowish white and finely granular.

The microscopic anatomy of neurofibroma is characteristic and distinct. The cells are long and spindle shaped, and have a tendency to arrange themselves in bundles which produce a palisade effect. This palisading of the cells is one of the main distinguishing features of the tumor. The nuclei run parallel in long columns, and each nucleus lies on top of another one. In a few other places one gets concentric whorls, as in a meningioma (14). The nerve cells and fibers which are present may be scarce in proportion to the stroma of the tumor and, hence, are difficult to recognize. Frequently the nerve fibers which are present may be so encroached on by the connective tissue that they become atrophic. Whenever the tumor arises from the specialized nerve tissue, it may approach the character of a neuroma, with a paucity of connective tissue framework. In other cases the tumor may arise from the connective tissue as a pure fibroma. In most cases, both connective tissues and nerve elements may be found, with the former in preponderance. In some tumors the stroma is extremely loose and myxomatous. Mitotic figures, and a marked change in the relationship of cells are seen in those tumors which are undergoing malignant degeneration.

Some idea of the difficulty in microscopic diagnosis encountered by those who are unfamiliar with these tumors is suggested by an incident in our series (Case 17). At operation, prior to the patient's admission to the clinic, the removed tissue was diagnosed in a state laboratory as malignant, and in another laboratory as "keloid-

Fig. 1. Case 16. Hæmorrhagic, cystic, degenerating neurofibroma.

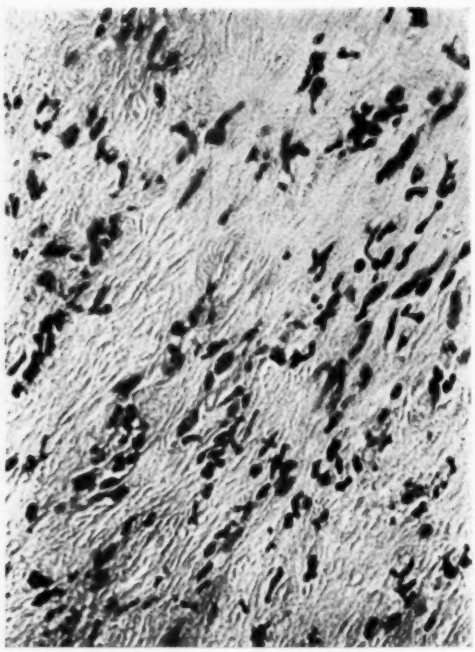

Fig. 2. Case 16. Neurofibroma, showing characteristic arrangement of nuclei.

like" tissue. On operation at the clinic for recurrence, the pathologist was unable positively to identify the type of tissue from frozen sections and could state only that it was not malignant, until fixed sections had been recognized as characteristic of neurofibroma.

SYMPTOMS AND SIGNS

The symptoms of neurofibroma of the neck are, as a rule, not severe. The patient generally seeks relief because of the disfiguration or the worry which the growth causes, rather than because of discomfort. Of our 17 patients 9 made no complaint of spontaneous pain. The 8 remaining made complaints of pain of varied intensity. One referred to his pain as a dull ache in the tumor; 2 stated that they had moderate discomfort, which was aggravated by fatigue; 1 stated that the tumor was sensitive to changes in the weather, and 1 had been symptomless for 8 years, at the end of which time the tumor had begun to throb like a toothache. In but 1 case was there any radiation of pain, and this only when the patient was fatigued, at which time the pain extended down to the shoulder.

Preservation of function of the affected nerve in cases of neurofibroma is rather remarkable. In none of our cases, even in those in which tumors were large, was there any evidence of impaired function of the nerve. It must be remembered, however, that none of the tumors in this series

arose from large sensory or motor nerves. Gatch and Ritchey also have observed that nerves will withstand much abuse from pressure and stretching by a benign tumor, but that malignant infiltration into the nerve fibers soon destroys their function. This is, in fact, the principal diagnostic feature of malignant degeneration of a neurofibroma, for sudden and rapid increase in size of the tumor is not proof of malignancy.

On physical examination, neurofibromata are, as a rule, discovered to be of rather hard consistency, to be regular in outline, and more or less freely movable. The tumors in all but 2 of our cases were described as being firm or moderately hard. One was described as being rather soft, and another, which had undergone cystic degeneration, was fluctuant. Three of the tumors were described as having a "malignant feel." All of the tumors were smooth, save two which were slightly nodular. The mobility of the tumors varied somewhat, but all were at least slightly movable. The cardinal sign of neurofibroma elsewhere in the body is limitation of motion in a direction parallel with the longitudinal axis of the affected nerve, whereas, there is freedom of motion transverse to the course of the nerve. This finding was not noted in a single one of our cases, probably because of the relative fixation of the surrounding structures, as well as the comparatively short course of the affected nerve between fixed points.

Although neurofibromata may cast a definite shadow in a roentgenogram (3) this shadow is by no means characteristic, nor could it be distinguished from the shadow cast by any other soft or firm tumor.

DIFFERENTIAL DIAGNOSIS

There are a few features in differential diagnosis which should lead to suspicion of the presence of neurofibroma, provided the condition is kept in mind as a possibility. The other tumors of the neck, from which it must commonly be distinguished, are the tumors resulting from lymphadenopathy, metastatic tumors, tumors of the salivary glands, branchial cysts, aberrant thyroid glands, tuberculomata, and such rarities as tumors of the carotid body. In but 5 of our 17 cases was a neurofibroma suspected before operation. None of these patients complained of neurologic symptoms, for the involved nerves in most instances were relatively unimportant sensory branches. Neurologic examination consequently was not as a rule carried out; the majority of the diagnoses were made in other than the neurologic section of the clinic. The operation was likewise as a rule done by a general rather than a neurologic surgeon.

To distinguish between neurofibroma and tumors resulting from lymphadenopathy is occasionally rather difficult. As a rule, however, when a tumor of the neck results from lymphadenopathy, study of the blood picture, the presence of enlarged lymph nodes elsewhere in the body and, particularly, detection of a discrete and separate mass making up the tumor of the neck, should lead to proper evaluation of the underlying condition, especially if one considers the lack of general symptoms and the paucity of complaints relative to the local condition in cases of neurofibroma.

The differential diagnosis between neurofibroma and metastatic carcinoma should offer little real difficulty. Although neurofibromata are firm tumors, and often are described as imparting to the touch a sensation like that imparted by malignant tissue, still they are, as a rule, more discrete, better circumscribed, more freely movable, smoother, and softer than carcinomatous nodes. The loss of weight and cachexia that accompany carcinoma are absent in neurofibroma, and of cardinal importance is the absence of any discernible primary source of malignancy. The age of the patient may be of some aid in making the distinction. Although 5 of our patients were more than 50 years of age when they were first aware of the tumors, the average age of the 11 remaining patients was but 26.4 years; the youngest patient in the group was 15 years of age, and the oldest, 44. The average age of the patients of the entire group was 34.8 years, which is definitely much younger than the average age of sufferers from carcinoma. These patients had known of their tumors for an average of about 6 years before they came to operation. The rate of growth is, as a rule, steady and gradual, although in one of our cases the tumor grew to the size of a fist within 18 months, and in 2 others the rate of growth was described as rapid. These features of slow growth and long duration should be very helpful in distinguishing neurofibromata from carcinomata, provided the patient has permitted himself to go for a long time without biopsy.

The distinction between neurofibroma and branchial cyst should be relatively easy unless, as in one of our cases, the neurofibroma has undergone cystic degeneration. Branchial cysts are, as a rule, encapsulated, discrete, fluctuant or cystic tumors, which may be freely movable or loosely attached to the deeper structures. Carp and Stout noted that a cold or sore throat fre-

quently preceded their appearance or increase in their size. Pain in branchial cysts is unusual.

Lateral, aberrant thyroid glands are, in reality, rather rare; hence, their diagnosis is difficult. This diagnosis was erroneously suggested in 2 of our cases. These tumors resemble neurofibromata in that often they do not cause symptoms, their growth is slow as a rule, and they are not tender. The consistency of aberrant thyroid glands is not constant; they may be firm or soft. Their only distinguishing feature is that they are likely to increase in size at puberty and to fluctuate in size during menses. These tumors are said by Lawton to be radiosensitive, and as this feature is not shared with neurofibromata, it might be of diagnostic aid.

The diagnosis of tuberculous lymphadenopathy usually can be made readily on the basis of presence of fever, positive tuberculin reactions, caseous lymph nodes or discharging sinuses. Neurofibromata may resemble tumors of salivary glands, especially those of the submaxillary glands. This resemblance appeared once in our series. In 3 of our cases (Cases 5, 6, and 7), there were small neurofibromata elsewhere in the body although the tumor in the neck in each instance was the predominant tumor. These cases of multiple neurofibromata fall into the classification of von Recklinghausen's disease.

TREATMENT

The treatment of neurofibroma is surgical removal as soon as the presence of the tumor is discovered. These tumors are potentially malignant, they will recur if not wholly removed, they are disfiguring, and in addition the difficulties in arriving at a correct diagnosis necessitate microscopic confirmation. These tumors are not radiosensitive; hence, roentgen-rays and radium are of no avail in treatment. Two of our patients underwent treatment by roentgen-rays prior to their admission to the clinic, without any appreciable effect on the neurofibromata. Flatau and Sawicki reported a case in which a neurofibroma was unaffected by both roentgen-rays and radium.

Surgical removal of neurofibromata should be instituted as early in the course of the disease as possible, for complete extirpation of the tumor means permanent cure. Delay in operation may permit such growth and extension of the tumor as to make complete removal impossible, and recurring tumors, necessitating repeated operations, will result.

Four of our patients had had neurofibromata incompletely removed before their admission to the clinic, with the result that secondary operations for recurrences were necessary. One of our cases represents well the danger of delay in surgical removal of these tumors. The patient first noted slight swelling in the neck in 1929. For 2 years she was given treatment with roentgen-rays and radium by her physician at home, after which surgical intervention was advised but complete removal of the tumor was not effected. The remaining tumor tissue increased in size more rapidly, and within 11 months it had reached the size of a hen's egg (about 6 centimeters in length), most of the enlargement having taken place in the last 4 months of this period. At secondary operation extensive dissection was necessary to remove the recurrent growth, which had extended underneath the internal jugular vein and the internal carotid artery, from its apparent point of origin in the descending hypoglossal nerve.

Neurofibromata should be completely removed because, in addition to the dangers of recurrence, there is also the inherent possibility of malignant degeneration. Although this phenomenon was not encountered in any of our cases, it is well vouched for in the literature. Gatch and Ritchey saw occasional mitotic figures, and a small portion which appeared to be a sarcoma, in a neurofibroma which they removed from a patient's neck. Gibberd reported an interesting case of Davies', in which a neurofibroma of the cervical sympathetic nerves was removed, and an adjacent lymph node was found to contain a deposit which was histologically identical with the main tumor. This patient had no signs of recurrence 3 years after the operation. Lemon, in speaking of mediastinal tumors, stated that neurofibromata of the mediastinum are potentially malignant in two ways: (1) they may take on periods of activity and grow to such an extent that they produce symptoms of pressure, and (2) they may become invasive, metastatic, and malignant in cellular characteristics and produce death in the manner of sarcoma. Gardner and Frazier, in tracing a family afflicted with a mendelian transmission of bilateral neurofibromata of the acoustic nerve, observed marked increase in malignancy with each transmission in the group. Whereas the members of the second generation averaged 72 years of life, those of the fifth generation averaged only 28 years. Flatau and Sawicki reported a cervical neurofibroma containing many mitotic figures. This tumor recurred a few months after its partial removal. Blodgett, Brough, and Lehman asserted that solitary neurofibromata have a marked tendency to undergo sarcomatous degeneration.

The technical difficulties met during operation may be great or small and often cannot be well evaluated before the incision is made. Frequently important structures must be sacrificed in the all important effort completely to remove the tumor. In this respect it may be wise to warn the patient of this possibility before operation. In but 6 of our 17 cases was the neurofibroma so situated and of such size as to be easily removed without considerable dissection to separate it from important structures. One was firmly attached to the floor of the mouth; 1 extended back of the angle of the mandible; 4 extended beneath the carotid sheath and were adjacent to the carotid arteries or internal jugular veins. One extended beneath the clavicle; 1 was beneath a submaxillary gland, which had to be sacrificed to effect removal of the neurofibroma. One was beneath the cervical nerves. Adson has given some valuable suggestions regarding the surgical procedure of choice in dealing with neurofibromata. He has recommended complete removal of the tumor including resection of the involved nerve (1) when the nerve is small and of no significance; (2) when the nerve is a sensory one, and (3) when the tumor is malignant. He recommended intracapsular removal of the tumor if it occurs in a mixed nerve and the tumor is benign. He stated that a fresh tissue study of the tumor before the completion of the operation is essential to determine the best operative procedure.

The complications of operation for neurofibroma of the neck lie mainly in destruction of the nerve from which the neurofibroma arises. One of our patients, whose neurofibroma arose from the cervical sympathetic nerves, had a Horner's syndrome after operation. This sequel also has been reported by Gibberd. Another patient, whose neurofibroma apparently arose from the left descending hypoglossal nerve, and extended into the carotid sheath, had contraction of the left pupil after operation. In another case, the neurofibroma had been thought, at operation prior to the patient's admission to the clinic, to arise from the left vagus nerve. On examination at the clinic, it was felt that the patient had an irritable heart resulting from sacrifice of the left vagus nerve. The left vocal cord was also fixed in the median line. After the recurring tumor had been removed at the clinic, slight left exophthalmos, but no Horner's syndrome, developed. The patient's voice improved surprisingly after removal of the tumor, which was pressing on the pharynx. Another patient, a man aged 26 years, had a very extensive neurofibroma in the right side of the neck, extending below the clavicle and into all fascial planes, and the spinal accessory nerve was intimately involved. Two years after operation the man was still suffering from some loss of function of the right arm, resulting from necessary sacrifice of nerves.

REPORT OF CASES

CASE 1. A man, aged 58 years, presented himself at the clinic in July, 1924. He gave the history that his father had died of carcinoma of the stomach. He stated that for 8 years a tumor had been present on the right side of his neck. The tumor had not caused symptoms; the rate of growth was not stated. July 21, a myxomatous neurofibroma, measuring 3 by 2 centimeters, was removed from the posterior triangle on the right side of the neck. In a letter dated August, 1933, the patient stated that the tumor had not recurred.

CASE 2. An unmarried woman, aged 22 years, came to the clinic in January, 1925. She stated that her brother had died of Hodgkin's disease. For the past 2 years, the left side of her neck had gradually increased in size. During the previous 2 months the growth had been a little painful. On examination, a firm, somewhat irregular, freely movable tumor was discovered in the left side of the neck. February 3, a neurofibroma, measuring 4 by 4 by 2 centimeters, was removed. Apparently it had developed in the left descending hypoglossal nerve and had worked its way beneath the internal jugular vein and internal carotid artery, the tumor apparently lying in the carotid sheath. There was contraction of the left pupil after operation.

CASE 3. A man, aged 35 years, was seen at the clinic in July, 1925. He stated that his mother and his grandmother both had died of carcinoma of the stomach. He gave the history that in 1921 one eye had been enucleated for melanotic sarcoma. At the time of his examination, a carcinoma of the rectum was found, along with some firm nodules in the left side of his neck. Biopsy of these nodules revealed neurofibroma. He subsequently successfully underwent operation for his rectal growth and apparently was in good health until March, 1932, when he died, presumably from metastasis of the carcinoma.

CASE 4. A man, aged 34 years, presented himself at the clinic in September, 1925. He stated that his mother had died of sarcoma. A tumor had been present on the right side of the neck for 8 or 9 years. He stated that the tumor had not increased in size during the past 6 years. On examination a hard nodule was discovered in the right anterior cervical region. The nodule seemed to be attached to the hyoid bone. At operation, September 5, the nodule was removed and was discovered to be a neurofibroma. In 1932, the patient was admitted to an asylum for the insane, but there apparently was no recurrence of the growth.

CASE 5. An unmarried woman, aged 18 years, came to the clinic in August, 1926. She stated that for 3 years a painless, slowly enlarging tumor had been present in the right side of the neck. The rate of growth had been unaffected by local applications of iodine. On examination, a firm, irregular tumor was discovered. The tumor apparently was attached to the spinal column. At operation, August 30, multiple neurofibromata were removed from the right posterior cervical region. The largest measured 7 by 1 centimeters, and the smallest, 3 by 4 millimeters. The tumor originated near the transverse processes of the fifth and sixth cervical vertebræ. In a letter, dated August, 1933, the patient stated that the tumor had not recurred.

CASE 6. A man, aged 51 years, entered the clinic in September, 1926. He stated that a tumor had been present in the right upper portion of the neck for 12 or 14 years, and had been increasing in size, but very slowly. The tumor gave no symptoms, and on examination was described as being rather soft. On September 14, a neurofibroma, measuring 8 by 5 by 3 centimeters, was removed from the right upper cervical region. The tumor extended back to the angle of the mandible. A small neurofibroma, measuring 2 by 1 by 2 centimeters, also was removed from the left thoracic wall. In a letter from the patient, received in August, 1933, he stated that the tumor had not recurred.

CASE 7. A man, aged 26 years, was seen in the clinic in January, 1927. He stated that his mother was suffering from a carcinoma of the stomach. He gave the history that for 4 years there had been progressive swelling of the right side of the neck. On examination a large, firm tumor the size of a grapefruit (about 12 centimeters in diameter) was found on the right side of the neck. There were a few, scattered, small subcutaneous nodules elsewhere on the body. At operation, January 17, a very extensive neurofibroma, weighing 240 grams was found. This tumor ran into all of the fascial planes below the clavicle and seemed to be attached to the side of the cervial portion of the spinal column. It was intimately involved with the spinal accessory nerve. Following operation there was some weakness of the right arm, resulting from the necessary sacrifice of nerves in removal of the neurofibroma. The patient's father, 2 years after operation, reported that the muscles of the patient's right arm still were somewhat weak.

CASE 8. A married woman, aged 57 years, presented herself at the clinic in January, 1927. She stated that her grandmother and one aunt had died from carcinoma. She gave the history that 9 years previously she had experienced some pain in the neck when her head was tilted backward. This pain had been of short duration at that time and she had been symptom-free for the following 9 years, until recently, when, in the back of her neck a pain had developed which she likened to a throbbing toothache. A small, movable tumor was palpable in the median line, over the sixth cervical vertebra. At operation, February 1, a neurofibroma measuring 1 by 1.5 centimeter, was removed from the ligamentum nuchæ. The tumor was very hard and fibrous and was well incorporated in fibrous tissue. In a letter received from the patient in August, 1933, she stated that the tumor had not recurred.

CASE 9. A boy, aged 15 years, was brought for examination in September, 1918. The history was that for a year the right submaxillary region had been gradually increasing in size. Apparently there had been remission in the rate of growth. The tumor did not cause symptoms, and on examination was found to be a discrete, moderately hard, barely movable mass, the size of a pigeon's egg (about 4 centimeters long). At operation, September 11, a neurofibroma weighing 70 grams was removed. It was situated in the right submaxillary space, displacing the submaxillary salivary gland downward and outward. It was firmly attached to the floor of the mouth; there was no line of cleavage. The patient returned to the clinic 8 years later, in 1927, and stated that during the past 2 years he had noted recurrence of the tumor. The rate of growth had been slow during the first year, and rapid during the last year. July 6, he was operated on again, and a large, recurrent neurofibroma, extending up to the base of the skull, was removed. August 16, he was again operated on, and a small, recurrent neurofibroma was removed from the floor of the right side of the mouth. He was given a course of treatment by roentgen-rays, and in a letter received in March, 1930, the patient stated that there had been no recurrence of the tumor.

CASE 10. A married woman, aged 58 years, entered the clinic in March, 1928. She stated that a tumor had been present in the left cervical region for 40 years. For 3 years it had not perceptibly increased in size, but in the past 8 months the rate of growth had been rapid. There had been no symptoms from the tumor. On examination, a firm, smooth, slightly movable tumor, with a "malignant feel," was found in the left side of the neck. At operation, March 6, a neuromyxofibroma, measuring 9 by 6 by 6 centimeters, was removed. It rose high behind the bifurcation of the carotid artery, and was pushing the artery forward. It was incorporated in the deep cervical fascia, was well encapsulated, and was easily enucleated. In a letter received from the patient in 1931, she did not mention recurrence.

CASE 11. A man, aged 50 years, presented himself at the clinic in March, 1929. He gave the history that for 4 or 5 years a swelling had been present in the left posterior cervical region. The swelling was sometimes tender. On examination it was discovered to be hard and discrete. On removal, March 12, the tumor was found to be a neurofibroma, measuring 2 by 1 by 1 centimeter. In a letter, dated August, 1933, the patient stated that the tumor had not recurred.

CASE 12. A married woman, aged 36 years, entered the clinic in April, 1929. She stated that her grandfather had had a carcinoma of the breast. For 9 years the patient had had a small tumor in the left side of the neck. The rate of growth apparently had been slow, but the patient thought that there had been some increase in size during her two pregnancies. Occasionally there was pain in the swelling, with some extension of pain down to the shoulder. On examination, the tumor was found to be firm, freely movable, and distinctly tender. At operation, April 10, a small, encapsulated neurofibroma, measuring 3 by 2 centimeters, was found in the posterior triangle on the left side of the neck. The tumor was freely movable, and was attached only to the fascia. In a letter received from the patient in August, 1933, she stated that the tumor had not recurred.

CASE 13. A youth, aged 18 years, presented himself at the clinic in June, 1929. He stated that for 2 or 3 months there had been a steadily growing, symptomless tumor at the right angle of the jaw bone. On examination the tumor was found to be hard, rather irregular, slightly movable, and situated at the right angle of the mandible. Two small lymph nodes were near it. The tumor was described as having a "malignant feel." At operation, June 9, a neurofibroma, measuring 5 by 3.5 centimeters, and weighing 30 grams, was removed from beneath the submaxillary gland, which had to be sacrificed. In a letter, received from the patient in August, 1933, he stated that the tumor had not recurred.

CASE 14. A married woman, aged 56 years, came to the clinic in December, 1931. She stated that for 2 years the right side of her neck gradually had increased in size. She experienced a sensation of strain in this region when she was tired. At operation, December 4, a myxomatous, degenerating neurofibroma was removed.

CASE 15. A married woman, aged 47 years, entered the clinic in August, 1932. She stated that in 1929 a tumor had developed in the left side of her neck. Growth of the tumor had been rapid and it had approached the size of a fist (about 8 centimeters in diameter) within 18 months. A course of treatment by roentgen-rays had been given elsewhere, without effect on the tumor, and in August, 1931, a huge neurofibroma of the vagus nerve had been removed elsewhere. Following this operation a good sized lump had remained above the scar, which had not increased much in size until April, 1932, when it had started

to grow, and had become the size of a hen's egg (about 6 centimeters long) by August, 1932, when she reported to the clinic. There was some pain when pressure was exerted on the growth, but otherwise there were no symptoms. The tumor had a "malignant feel" and was slightly movable. The left vocal cord was fixed in the median line, and an irritable heart and rapid pulse were felt to be results of sacrifice of the vagus nerve at the previous operation. The patient was operated on at the clinic on August 4, and a very large neuromyxofibroma, measuring 9 by 6 by 4.5 centimeters, was removed. It apparently arose from the third cervical sensory nerve and necessitated wide dissection for its removal. The carotid vessels, the mucous membrane of the nasopharynx, the carotid gland, and the transverse cervical processes were exposed during its removal. After operation there was slight left exophthalmos, but no Horner's syndrome. In a letter, received from the patient in August, 1933, she stated that she was in good health and that her voice was improving.

CASE 16. A married woman, aged 38 years, was admitted to the clinic in October, 1932. She stated that her mother had had a carcinoma of the uterus. She gave the history that for 4 years there had been progressive swelling of the left side of the neck. This had been diagnosed tuberculosis elsewhere, and a course of treatment by roentgen-rays had been given without any effect on the tumor. The patient complained of a drawing sensation in the neck, and stated that it was sensitive to changes in the weather. On examination, the tumor was found to be smooth, movable, and slightly fluctuating. At operation, October 21, a deeply placed, hæmorrhagic, cystic, degenerating neurofibroma was removed without rupturing it (Figs. 1 and 2). A left Horner's syndrome developed postoperatively.

CASE 17. A girl, aged 3 years, was brought to the clinic in April, 1933. Her mother stated that in January, 1932, the patient had fallen and had struck her neck. A short time afterward, a firm mass had been felt in the injured region. An ointment had been applied, but the mass had continued to increase in size, and in November, 1932, elsewhere, the tumor had been removed. The tissue had been reported to be malignant by one laboratory and of a keloid nature by another. The tumor reappeared in January, 1933, and continued to grow until April 10, 1933, when at the clinic, a hard, somewhat movable, recurrent tumor measuring 3 by 3 centimeters, was cleanly removed from the left upper cervical region. A drainage tube was left in place, through which irradiation with radium was instituted. Microscopic diagnosis of the tumor, by frozen section, revealed a benign tumor, the exact nature of which could not be ascertained. Fixed sections disclosed that the tumor was a neurofibroma. In a letter from the mother, received in October, 1933, she stated that the tumor had not recurred.

CONCLUSIONS

We have attempted to emphasize certain important points relative to cervical neurofibroma, as follows: (1) the hereditary factor in the etiology of neurofibroma of the neck cannot be lightly disposed of, even though it is not proved; (2) a wide variety of nerves in the cervical region may be affected by neurofibroma; (3) neurofibromata are potentially malignant; sudden increase in rate of growth or long duration are not necessarily criteria for malignant change; (4) differential diagnosis is usually made from the various forms of lymphadenopathy, metastatic tumor, tumor of the salivary glands, branchial cyst, aberrant thyroid gland, tuberculoma, or tumor of the carotid body; (5) results of treatment by roentgen-rays or radium have not been satisfactory; (6) treatment of cervical neurofibroma is radical surgical removal.

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THE TOXÆMIAS OF PREGNANCY[1]

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THE toxæmias cause the death of approximately 4,000 women in the United States each year. The general mortality in eclampsia is 20 per cent; therefore, at least 20,000 women must have the disease each year. The ratio of eclampsia to the larger group of non-convulsive toxæmia varies from 1 to 5 to 1 to 15; therefore, at least 100,000 women each year in the United States have their pregnancies complicated by toxæmia. All follow-up studies indicate that many of these toxæmic women are partly incapacitated or that their life expectancy has been definitely shortened because of irreparable injury to the kidneys, vascular system, or heart.

During the past 9 years I have been interested in the toxæmias of pregnancy and have made various investigations. I have done experimental work on both humans and animals. These studies were started with Dr. Schwarz in St. Louis and have been continued in Chicago with Dr. Adair and Dr. DeLee. I have had unusual opportunities to examine, study, and treat at least 700 toxæmic patients, of whom 75 had eclampsia. Prior to 1934 we had examined 3,688 samples of blood from approximately 400 toxæmic patients. Each specimen was analyzed on an average for twelve substances, and special emphasis was placed on repeated determinations on the same patient. About 2,000 specimens of urine from approximately 300 patients also have been analyzed for various constituents.

Many obstetricians state that we have learned nothing concerning these diseases but a brief résumé of the more important data, obtained by chemical analysis of the blood and urine, various renal function tests, follow-up studies, and observations on large groups of patients treated with definite routines, indicate that our knowledge of the toxæmias of pregnancy is increasing slowly.

Repeated chemical analyses of the blood of these toxæmic patients indicate that:

The alterations in blood and plasma volume in eclampsia and pre-eclampsia, as indicated by changes in serum protein, hæmatocrit and hæmoglobin determinations, are identical, thus linking these two conditions together and definitely separating them from the patient with nephritic toxæmia or essential hypertension.

In the majority of patients with œdema, the internist usually believes that its presence is due to a low serum protein. Practically all of the patients with toxæmia of pregnancy have a serum protein above 5 grams per cent and although the albumin fraction is lowered, the decrease is not sufficient to be the cause of the œdema.

Despite the high blood pressure, œdema, albuminuria, and other signs of kidney involvement, we found that in about 3,700 analyses of blood, the non-protein nitrogen was 40 milligrams per cent or more in only 67 blood specimens from approximately 20 patients. The toxæmia is not due to a retention of urea, uric acid, creatinine, or amino-acids.

The hæmoglobin is a little less than the average normal for pregnancy and decreases still more after delivery. Venesections are therefore not only contra-indicated but actually dangerous.

The acid base balance is altered slightly but because of compensatory changes there is no danger, as a rule, of acidosis or alkalosis.

With the exception of hæmoglobin, the routine determination of all blood constituents is useless. Each patient presents a different problem and if chemical examination of the blood is thought advisable, specific determinations should be made.

Examination of the urine indicates that:

The pregnant woman, probably because of the excess of amount of water in her tissues (physiological œdema), is able to excrete urine with an average specific gravity of only 1.022 after a 15 hour fast. With longer fast periods or after delivery or death of the fetus, she is able to excrete urine with a specific gravity of 1.030 or even higher. The average specific gravity for the toxæmic patient is approximately 1.013. As a rule, if the patient is able to excrete urine with a specific gravity of 1.010 or more and the 24 hour volume of urine is 1,000 cubic centimeters or more, the blood non-protein nitrogen and urea nitrogen will not be increased. When the 24 hour volume of urine is less than 1,000 cubic centimeters and the specific gravity is less than 1.010, it is advisable to determine the non-protein nitrogen.

The microscopic examination of the urine, if done by the Addis method, which entails the examination of the sediment from a concentrated specimen collected over a known period of time, has been of the utmost value for diagnosis, prognosis, and treatment.

[1]Read at a meeting of the Chicago Gynecological Society, January 19, 1934.

The phenolsulphonephthalein test in approximately 60 toxæmic patients was less than 50 per cent for a 2 hour total in only 5 cases, and has not been used by us since 1929.

The urea concentration in the urine after the administration of 15 grams of urea by mouth in approximately 50 toxæmic and normal pregnant patients was rarely over 2 per cent (normal 2 to 4 per cent) and, therefore, this test is no longer used by us.

The urea clearance test of Van Slyke has been used about 400 times in 150 patients. We are attempting to determine its value at present. We can state, however, that if the clearance is determined after delivery and found consistently to be less than 20 per cent of the normal, we know that the life expectancy of the patient is but a few years at the most.

The determination of the glomerular filtrate by the Rheberg creatinine method has been used in too small a number of patients to warrant any conclusions.

The kidneys of many eclamptic and pre-eclamptic patients function normally within 24 hours post partum, thus precluding any organic lesion and presupposing a functional one. A spasm of the arterioles, decreasing or even stopping the blood flow through the glomeruli, would explain many of the findings and would, if continued too long, result in permanent kidney pathology and decreased function.

We believe that the toxæmic patients should be considered as a group and that they should be divided arbitrarily into convulsive, or eclampsia (convulsions and/or coma), and non-convulsive toxæmia. The latter group is composed of all patients who have albuminuria, hypertension, or œdema during pregnancy. The parity of the patient, history, time of onset of symptoms, various blood and urine examinations, and renal function tests, especially several weeks or months after delivery, are considered in deciding whether or not the condition was one of pre-eclampsia, pregnancy with chronic nephritis, or essential hypertension. The data obtained in the laboratory are considered in arriving at a final diagnosis, but they do not make the diagnosis. We believe that the patient with the so called low reserve kidney either has a chronic nephritis or an essential hypertension. The statement made by some observers that the condition does not progress is open to criticism. The very fact that this statement is made implies periodic observation of the patient, which means constant supervision of diet, rest, and elimination. In addition, the large inherent technical error in the various tests may mask the damage to the cardiovascular renal system which each pregnancy undoubtedly is producing in these patients. It is a common observation by internists that rest, diet, and elimination seemingly will arrest and many times apparently cause improvement in patients with nephritis or hypertension.

An examination of the past obstetrical histories of many patients, who die during or shortly after labor without an apparent primary cause, indicates that these patients usually had mild symptoms of toxæmia with each pregnancy. The result of the repeated toxæmias has been a slightly damaged heart or kidney, or an anæmia. An additional strain, such as a prolonged labor, hæmorrhage, infection, or a mental shock has been the proverbial straw which broke the camel's back. The prevention of future pregnancies and the treatment of the anæmia or the cardiovascular system would undoubtedly have prolonged these patients' lives.

Vasomotor lability appears to be a significant index of diagnostic and prognostic value. This is determined by permitting a patient, under basal conditions, to immerse her hand in water at plus 1 degree centigrade and observing the fluctuations in blood pressure every 30 seconds for 2 minutes. If, after repeated tests, the systolic blood pressure shows a rise of 40 millimeters of mercury or more before or after delivery, the patient has an impaired vascular system which may or may not involve the kidneys.

In Table I are summarized the number of severe and moderately severe toxæmic patients admitted to the Chicago Lying-in Hospital over a period of 2 years and 7 months. During this time there were 6,968 deliveries exclusive of abortions. There were 327 hysterotomies during this period; the majority, of course, were cæsarean sections of the laparotrachelotomy type.

The number of toxæmic patients is large (6.7 per cent) in proportion to the number of deliveries, even if the number of home deliveries is included. There were 4 immediate deaths, 2 of which were from hæmorrhage (private patients), 1 from infection, and 1 from an acute nephritis with infection, who died undelivered. The low maternal mortality is due to an early termination of pregnancy, either by induction of labor or cæsarean section if near term, or by hysterotomy if discovered early in pregnancy. Thus, in 196 patients (45 per cent) labor was induced or the pregnancy terminated by an operative procedure. If labor cannot be started by medical means, our results seem to indicate that the insertion of a bag and/or rupture of the membranes are the most efficacious methods.

TABLE I.—NON-CONVULSIVE TOXÆMIA OF PREGNANCY. CHICAGO LYING-IN HOSPITAL OVER A PERIOD OF 2 YEARS, 7 MONTHS. ONSET OF LABOR, VARIOUS METHODS OF INDUCING LABOR AND TERMINATING PREGNANCY

		Total
Number of patients		438
Number of maternal deaths		9
Within 2 weeks postpartum	4	
Within 6 months postpartum	4	
Within 1 year postpartum	1	
Number of fetal deaths, after 8 weeks' gestation		35
1. Spontaneous onset of labor		241
2. Induction of labor		106
Medical	34	
Ruptured membranes	20	
Intra-uterine gauze packing	17	
Intra-uterine bag	23	
Intra-uterine gauze, bag	8	
Intra-uterine gauze, ruptured membranes, bag	2	
Ruptured membranes, bag	2	
3. Therapeutic abortion		3
4. Laparotomies		85
Indications: Toxæmia + contracted pelvis, previous cæsarean section, premature, postmature, abruptio placentæ		

Weight of fetus		*Number of fetal deaths*
5000 grams or over	1	
4000–4999	6	
3000–3999	16	
2000–2999	34	
1500–1999	11	1
1000–1499	1	1
– 999	15	16
Total		18

Hysterectomies		9
Porro cæsarean sections		3
Vaginal hysterotomies (1 mole)		2
Sterilized		48
Maternal deaths		2
Within 2 weeks postpartum	1	
Within 6 months postpartum	1	

There were 85 laparotomies done on toxæmic patients, the majority of whom had severe symptoms. The indication for the laparotomy was rarely the toxæmia *per se*. Usually, contributory factors were present as indicated. There was only one immediate death, which occurred in a toxæmic patient who had a complicating cardiac decompensation, and several of us believe that the patient might have survived if the operation either had been delayed or not done. In this operative group, only one baby, weighing over 1500 grams, was lost. These babies usually are premature, maybe toxic, and in many cases are more valuable to the parents than babies of patients without toxæmia. We ascribe the low fetal mortality to the minimal birth trauma produced by cæsarean section, as contrasted to the physiological trauma (Ehrenfest) produced by delivery through the natural passage. The prevention of future pregnancies by operative sterilization was an additional indication in a number of cases. We believe that in these patients, because of the unreliability of contraceptive methods, one is often justified in subjecting them to the additional risk of a laparotomy. A small number of pregnancies was terminated and the patients sterilized by hysterectomy. This certainly is the easiest and safest method, but it seems to me that these patients maintain a higher blood pressure and have more headaches and other minor disturbances than those sterilized by tubal resection.

The general plan of treatment for the non-convulsive toxæmia of pregnancy is as follows:

Rest. We advise absolute bed rest with the additional use of sedatives, such as luminal, bromide, amytal, etc.

Diet. Limitation of protein, fat, and salt. The fluid balance is watched carefully. The urine should form at least 80 per cent of the intake. *Types of diet.* For the eclamptic the diet consists of fruits and fruit juices. This is an alkaline diet because of the high content of potassium and sodium. It can be maintained from 5 to 10 days and is used in severe cases. As a rule, no limit is placed on the intake unless there is some evidence of cardiac decompensation.

For the pre-eclamptic, the diet consists of protein (60 grams), fat (30 grams), carbohydrate (400+ grams), and is salt poor.

For the patient with nephrosis the diet is similar to that for the pre-eclamptic, except that the protein content is increased to 100 to 150 grams. This diet is used if there is a marked albuminuria (5 grams or more per 24 hours) over a long period of time. Rarely used during pregnancy.

Drugs. Luminal is given in doses of ¼ to 1½ grains three times daily, by mouth; sodium luminal, in doses of 2 to 5 grains, subcutaneously, two or three times daily if convulsions seem imminent.

Elimination. Magnesium sulphate, 60 cubic centimeters of a 50 per cent solution, is given by mouth and not repeated. Enemata of 180 cubic centimeters of a 50 per cent solution are used if œdema is marked. Cascara, phenolphthalein, or some other mild cathartic for daily use.

Œdema. Eclamptic diet is adhered to and the water balance maintained. Occasionally fluids are limited to 1,000 cubic centimeters, or even 800 cubic centimeters, per 24 hours. Salyrgan and novasurol have been of no value. Ammonium chloride or nitrate in 6 to 10 gram doses daily has been of use.

Oliguria or anuria. The intravenous injection of hypertonic glucose solutions:

Usually 500 cubic centimeters, of a 20 per cent solution, is administered over a period of from 30 to 60 minutes and repeated two or three times daily. Occasionally 1,000 cubic centimeters of a 20 per cent solution is used.

If the 20 per cent solution fails to produce a diuresis, from 500 to 800 cubic centimeters of a 30 per cent solution is injected two or three times daily.

In patients with anasarca or with cardiac decompensation, from 100 to 200 cubic centimeters of a 50 per cent solution is injected two or three times daily.

Gum acacia solution: If a diuresis cannot be produced with glucose solution the injection of from 500 to 1,000 cubic centimeters of a 6 per cent acacia in normal saline is of value.

Magnesium sulphate solution: The slow intravenous injection of from 100 to 200 cubic centimeters of a 2 per cent solution is of value in producing a diuresis if glucose injections fail.

Venesection and plasmapheresis are no longer used.

In Table II are summarized the data for the eclamptic patients. There were only three cæsarean sections, with a questionable indication for one, performed in 15 antepartum cases of eclampsia. The one maternal death occurred in a patient who walked to the delivery floor at 3:30 p.m., began having convulsions at 4:00, and died at 5:00 p.m.

Of the 438 toxæmic patients, 90, or 20 per cent, gave a history of previous toxæmia. Twenty-nine patients who gave a history of convulsions in a previous pregnancy were delivered by us, and 26, or 90 per cent, had some evidence of toxæmia in the present pregnancy.

In general, the rules which we attempt to follow are:

If the pregnancy is less than 28 weeks' gestation, and, if after a period of from 7 to 10 days' observation, study, and treatment, the symptoms and signs continue or become worse, the pregnancy is terminated. If the patient has one child or more, we advise against future pregnancies if postpartum studies indicate a permanently impaired cardiovascular renal system.

If the patient is seen after the period of 28 weeks' gestation, and, if after from 7 to 10 days' observation and treatment, there is no improvement, the pregnancy is terminated. However, if there is any amelioration of the signs and symptoms with bed rest, diet, elimination, and sedatives, no interference is indicated. Many of these patients can be carried to term and delivered through the natural passage.

An increase in blood pressure, in the amount of albumin or œdema, a decrease in visual acuity or amaurosis, jaundice, or the development of an oliguria or anuria warrants immediate termination of pregnancy.

The occurrence of convulsions in association with other evidence of toxæmia warrants the termination of pregnancy unless the fetus dies *in utero*. I have not seen or read reports of a true case of severe intercurrent eclampsia in which the baby was born alive.

I believe that we will always have toxæmias of pregnancy, but proper rest, elimination, and diet will reduce the incidence. Preconceptional, prenatal, and postnatal care are of the utmost value in lowering the incidence and mortality of toxæmia.

TABLE II.—ECLAMPSIA. CHICAGO LYING-IN HOSPITAL OVER A PERIOD OF 2 YEARS, 7 MONTHS. DELIVERIES—6,968 WITHOUT ABORTIONS—WITHOUT HOME SERVICE

	Total	Private	Ward
Number of patients	30	4	26
Mild	19	4	15
Severe	11		11
Antepartum	15		15
Postpartum	15	4	11
Induced labor	14	2	12
Cæsarean section	5	1	4
Mortality			
Maternal	1	0	1
Fetal	3	1	2

The mortality due to the toxæmias of pregnancy will not be decreased until a rational campaign, even more widespread than that devoted to cancer, is instituted. The public then will become cognizant of the extreme importance of the toxæmias of pregnancy, and funds and material will become available for study. Because of the relative scarcity of patients, the research work will have to be carried out in the various cities and districts in specified hospitals, according to designated plans suggested by a central organization, whose membership may be composed of men selected by the various medical schools and special obstetrical societies. Thus, within the period of 1 or 2 years, all of the various types of therapy can be tried out and the most efficacious instituted with a resultant decrease in mortality. Similarly, the various theories, as to the etiology, can be investigated on a scale large enough to indicate their value. Within 10 years the cure, cause, and prevention of eclampsia and allied toxæmia would be known.

EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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OCTOBER, 1934

THE BATTLE OF THE PROSTATES

SOMETHING over a year ago I made bold to suggest in these columns that the transurethral method of attack upon the obstructing prostate had achieved an important position in the field. I suggested at that time that the procedure was surrounded by technical difficulties, and that there was grave danger that in inexperienced hands disaster would occur. I further expressed the apparently futile hope that the operation would be allowed to develop naturally and be not too generally adopted. A year has now elapsed, and we are in a position further to survey progress.

In its recent developments two types of technique have been used: one what may be called the Young, Caulk, Bumpus type, the other, the Stern, Davis, McCarthy type. The former method depends upon cutting away portions of the prostate with a circular knife introduced through the sheath, the bleeding being controlled by touching up the bleeding points under sight. This method involves a minimum of coagulation of tissue. The latter method depends upon the removal of tissue by means of a wire loop charged with a very high frequency current. Bleeding is further controlled by direct coagulation. It will be noted that in the first of the two types there is relatively little coagulation, and consequently relatively little danger of deep necrosis, which may later be followed by secondary hæmorrhage when the slough separates. In the second method, particularly in the hands of a less skilled surgeon, relatively large amounts of coagulation may occur, causing the death of a considerable amount of tissue which is not removed.

During the last year these operations have been very extensively employed. The Davis-McCarthy method has been selected by the majority of operators because the instruments used are similar to the cystoscopes with which they are familiar, and it does not therefore require the learning of new methods. The Caulk-Bumpus method utilizes instruments with which few even trained urologists are familiar, and which they are therefore reluctant to use. A survey of the last year's work in this country appears to me to warrant the conclusion that in the hands of those previously experienced the operation has lived up to its promise. On the other hand, as was to be feared, there have come from many quarters reports of poor results and serious accidents centering chiefly around the two complications of secondary hæmorrhage and infection. It is proper, perhaps, to call attention to the fact that these have been the two most serious stumbling blocks in all previous operations for prostatectomy. They are simply re-appearing here in another form, chiefly in the hands of the inexperienced.

The occurrence of these accidents does, however, call attention sharply to the necessity of graduate training even for those who are already expert in the field of urology. It proves beyond a doubt that these operations can be satisfactorily done only by experts, and should be attempted by no others.

It is unfortunate that the success of this operation in capable hands has led to the unwarranted assumption that it can be satisfactorily carried out by surgeons familiar with cystoscopic manipulations, or even by physicians with no such experience. Obviously, all of the knowledge and experience which have proved essential to successful prostatectomy by other methods are required here. Mere technical dexterity in transurethral instrumentation will not insure against the complications referred to, nor will they avoid the danger of operating upon the patient insufficiently prepared. It is, I think, safe to assert that the success of this operation will depend upon a sound training in the surgery of the bladder, upon supervised training in the technique of the methods of operation, and on a sufficiently large experience to enable the operator to become thoroughly familiar with the technique. Obviously the operation can be satisfactorily done only by qualified experts. Its performance by those of lesser qualifications will lead, as during the last year, straight to disaster.

HUGH CABOT.

CROSS GRAFTING OF ENDOCRINE TISSUES

FAR in the unrecorded past, mankind held the belief that by absorbing into his own body certain tissues of other animals he could acquire the qualities that he attributed to those tissues. The savage ate the heart of the lion to gain the lion's courage. Surgeons have many times attempted to follow the same idea in a less naïve manner, seeking to graft the tissues of one individual into the body of another. A limited success has followed some of these experiments. When the grafted material has been used for structural replacements—as for instance to repair defects of bone or tendon—it has many times served a useful purpose. The belief is, however, that not the living cells of the graft survive but merely their non-living scaffolding like the calcium frame-work of bone or the collagenous fabric of tendon or fascia. Into this the living cells of the host penetrate and either incorporate it or slowly replace it.

But when it comes to an actual maintenance of living, growing, and functioning cells in the body of another animal, success has been very rare. Yet, could such transplantations be accomplished, they would offer a therapeutic method of great possibilities. There are numerous disorders in which not a structural but a chemical deficiency is present, as best exemplified by lesions that have destroyed essential endocrine glands. Here the replacement of the lost tissue by living cells from another healthy gland would correct the condition. There have been isolated reports of occasional success in such grafts, but the great majority of attempts have failed. The writer and his associates have been working for several years in order to develop a method for such cross grafts and at the present time have reached at least a measure of success. The details of this work are reported elsewhere. Certain principles have emerged in the course of this study:

The location in which the graft is placed is important. It should be close to a good blood supply but not in tissue with a dense capillary network, as in such tissue hæmatoma interferes with the success of the graft. The tissue should be loose, without a dense enclosing sheath or capsule that would inhibit the growth of the graft by pressure. The location should

be easily accessible and, of course, should not be a structure important to life. The axilla and the groin meet these requirements.

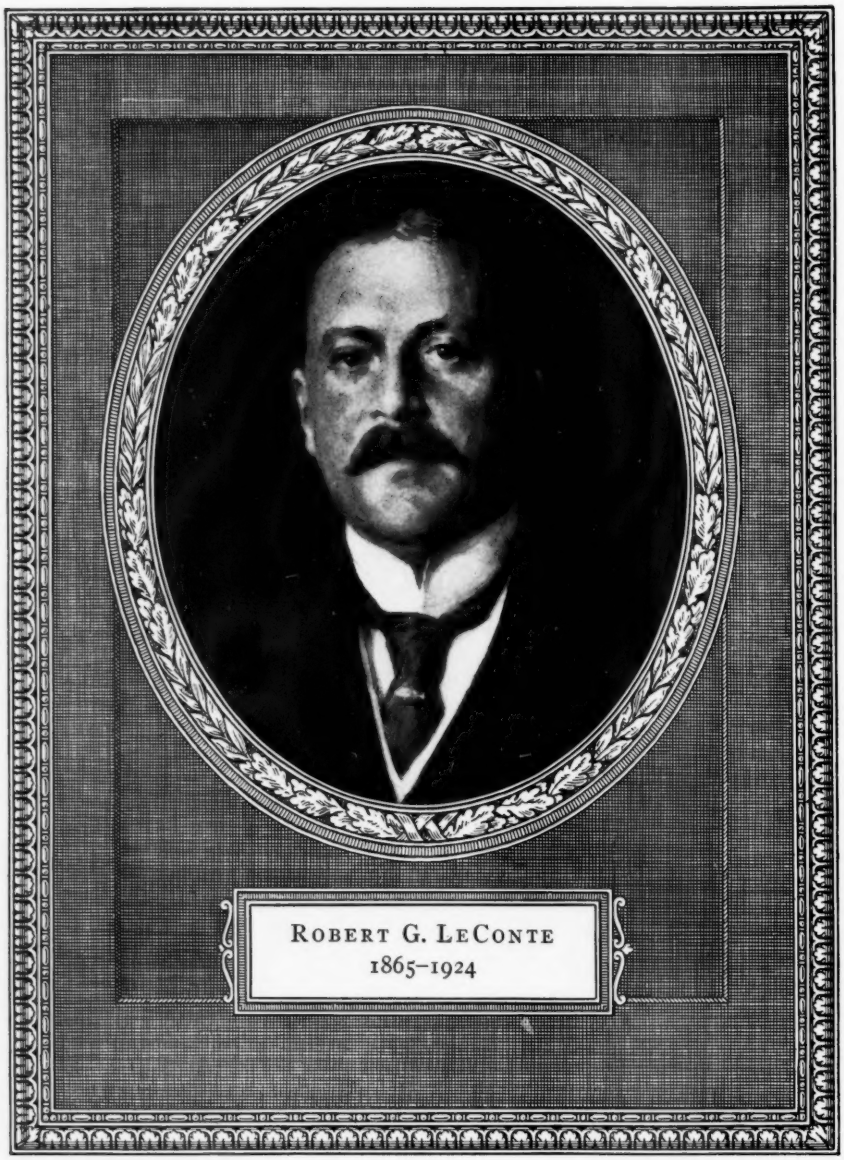
The size and form of the graft are important. The cells must live by osmosis and diffusion during the interval between their implantation and the development of an organized blood supply from the vessels of the host. Experience has shown that only a few layers of cells on the periphery of the graft can be so sustained and the central areas undergo necrosis. Hence numerous, very tiny fragments of tissue, or better still, the spread out sheets of cells in tissue cultures of the graft afford the best physical form for survival.

The adaptation of the graft to the specific chemistry of the host animal is important. Clinical experiments in grafting skin from one human being to another have frequently looked most promising for a period of 10 days to 2 weeks but rarely have been permanent. They begin to disintegrate after the first apparent take and usually are completely gone in 3 to 4 weeks. This and other such failures have been regarded as evidence that the graft could not thrive in the alien chemical environment of its new host. In the effort to meet this difficulty we have grown the fragments of endocrine glands to be grafted, in tissue culture on a medium containing the serum and plasma of the future host. A period of 2 to 4 weeks of such preparatory tissue culture has been employed.

It is probably necessary for the success of a graft that the animal receiving it be deficient in that particular type of tissue. This is the so called Halsted "law of deficiency." Whether or not this is universally true we cannot say, but it is true that in all of our experimental animals there has been created a deficiency before the grafting, and all our human cases were presumably deficient also. The quality of the tissue grafted is important. There is apparently a difference in the vitality and growth potential of tissue obtained from young animals as compared with old. A parallel factor concerns the age and general health of the host animal. Likely the chances of success are greater when the recipient is young and healthy except for the specific glandular deficiency for which the grafting is performed. Numerous other elements entirely unknown to us enter into the success or failure of cross grafting.

As a result of the application of the principles just outlined a promising measure of success in cross grafting of parathyroid and thyroid tissue has been attained. In a series of dogs about 45 per cent of definitely successful grafts of thyroid tissue was finally attained after many earlier failures. No grafts were considered successful when less than 4 weeks old, and some of these grafts were removed as late as about a half year after implantation and found vigorously healthy and apparently growing. The same method has been applied to human patients deficient in thyroid and parathyroid tissue. Most of these cases are too recent to permit conclusions, but two cases, at least, now over a year since grafting, seem to be successful. In estimating the value of any grafting method, it must be borne in mind that even in the simplest form of transplantation of tissue, namely the moving of skin from one part of the same individual to another part, there is not an infallible 100 per cent of takes. With the additional complication and difficulty of cross grafting it is scarcely rational to expect that any method may be evolved that will not be marred by a certain number of failures. It would obviously be a mistake, therefore, to expect too much from the work herein discussed, but it is equally obvious that some of the interesting problems concerned in cross grafting are repaying investigation. The great clinical and biological interest of the subject surely justifies further study.

HARVEY B. STONE.



ROBERT G. LECONTE
1865–1924

UNIV. OF MICH.

MASTER SURGEONS OF AMERICA

ROBERT G. LECONTE

ROBERT G. LECONTE was one of the best known and most highly respected American surgeons, in character and ability sustaining the reputation of Philadelphia surgery. Dr. LeConte was born in Long Branch, New Jersey, in 1865; he died in Philadelphia August 3, 1924. The LeConte family were French Huguenots. His father, Dr. John L. LeConte, was a well known entomologist and a distinguished member of the Academy of Natural Sciences of Philadelphia. As a child, LeConte was sent to school in Switzerland where he acquired an excellent facility in the French language which proved of great use to him in his subsequent career; in fact, on his return to America, he spoke French much better than he did English. He received his degree in Arts and in Medicine from the University of Pennsylvania, graduating in the medical class of 1888. During his undergraduate days he was an office student of the late Dr. W. W. Keen. He served his internship at the Pennsylvania Hospital, and throughout his career, was continuously on the staff of that institution, being made attending surgeon on the death of John Ashhurst, a position which he held up to the time of his death. For many years he was also surgeon of the Children's Hospital. Later he served as trustee of the University of Pennsylvania, of the Wistar Institute, of the Drexel Institute, and was on the Board of Managers of the Zoological Society.

In the surgical world, LeConte was generally identified with the Pennsylvania Hospital, because it was here that his most distinguished surgical work was done. He succeeded Dudley Allen as secretary of the American Surgical Association; he held the position for 8 years and was made president in 1915. He was one of the original group of the Society of Clinical Surgery. In neither of these organizations was there a more popular and beloved member than Bob LeConte.

As an operator, he was both careful and skillful and his patients and all who worked with him were devoted to him. He was always cheerful, optimistic, and encouraging. His two outstanding characteristics were his kindliness and charity. New acquaintances soon became admiring and devoted friends.

His social charm put him much in demand, and for many years he was the most popular bachelor in Philadelphia. He was a member of all the élite social organizations in and about Philadelphia and was a connoisseur of both food and drink. He also took an interest in all sports, but was never himself athletic. He

was probably fonder of aquatic, than of field, sports. He sailed in the Transatlantic Yacht Race of 1904, crossing in Stimson's *Fleur de Lis*.

When the United States became a participant in the World War, LeConte very naturally entered the medical service of the Navy where for the next two years he did conspicuous work. His knowledge of French served him well and he became in a sense a kind of liaison officer with a roving commission which permitted him to visit practically all of the British, French, and American hospitals and report on their activities. After the War he returned to Philadelphia and resumed his surgical work.

On May 24, 1916 he married Mrs. Antonio Y. Stewart of Philadelphia who survives him.

The accompanying photograph is of an excellent portrait by Julian Story, now hanging in the Pennsylvania Hospital.

To all of his friends he was known as "Bob" and the abbreviation meant more than intimacy, it meant affection.

JOHN H. GIBBON.

EARLY AMERICAN MEDICAL SCHOOLS

THE COLLEGE OF MEDICINE, UNIVERSITY OF CINCINNATI 1820–1934

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THE history of the Medical College of Ohio is so interminably interwoven with the name of Dr. Daniel Drake, the founder, that any reference to the college immediately excites recollections of this mental giant in the minds of those familiar with the history of this institution. Drake's objective was that of a loyal, patriotic citizen to the city of his adoption when he set about founding a medical school in Cincinnati and to make this city a center for teaching science and literature. Legal requisites were readily obtained from the Ohio State Assembly after Drake presented before this body his vision of the inestimable benefits which would accrue if his proposal were adopted.

Doctors are notably poor organizers; in this phase of founding the College, Drake was either badly advised or inadvertently committed the error of selecting members of the faculty as trustees of the institution, endowing them with full power to select and dismiss members. Jealousies and imperfections of the race of man were rampant in those far off days, even as they are today, the blood stream ran hot, fire coursed through the veins, the *code duello* was in flower and it required all the sagacity and ingenuity of this master mind to cope with such defects before success crowned Drake's efforts in his great undertaking.

Western people at that time looked to the East for erudition, skill, and science; the practice still smoulders, occasionally bursting into bright flame and sometimes defeats a laudable purpose in educational fields.

In selecting members for the faculty, Drake *imported* two doctors from the East, "a process which, though sometimes successful, is oftener attended with disappointment."[1]

Drake appealed only to men of ability, character, and public spirit, as he supposed, to become his associates in the college and although he knew much of the ills, frailties, and cupidity of mankind in general, he knew practically nothing of the disposition of doctors. While some one has aptly said that principles not men, another modifying this maxim, that principles *and* men are requisites, experience in affairs human leads one to conclude that men mean practically everything, methods very little, in teaching or practicing the science and art of medicine.

Drake, this far-sighted man, visualized the urgent necessity of a hospital in connection with the college for the purpose of bedside teaching and the Commercial Hospital and Lunatic Asylum, the forerunner of the present 1,800 bed Cincinnati General Hospital, was organized and opened to the students. The immortal Gross said of Drake, "No man could be in his presence without feeling in contact with a man of superior intelligence and acquirement."

In his memorable address at the opening of this hospital, Drake spoke as one inspired, in the following prophetic words: "The time has passed by when students will flock to men of genius for the purpose of listening to expositions of theory or to be amused with creations of imaginations. The school which is not based on a hospital may have learned and able professors; but the results of their teaching can never be satisfactory to the student who seeks to make himself a good, practical physician and surgeon. For in the hospital the student learns pathological anatomy, diagnosis, the art of prescribing, and operative surgery."

A charter was granted to the Ohio Medical College by the State Assembly, 1818–1819, and the first course of lectures was delivered in 1819–1820, by a faculty consisting of three members to twenty-five students. Drake was president of the faculty and filled the chair of theory and practice, obstetrics, diseases of women and children. When enthusiasm, co-operation, and integrity are wanting, the most noble intentions and best planned

[1]Mansfield, Edward D., Memoirs of the Life and Services of Daniel Drake, M.D.

University of Cincinnati, College of Medicine

enterprise is doomed to failure; advancement in literature, art, ethics, and science are usually neglected by persons devoid of taste, imagination, and vision, thus through the ages has knowledge been retarded by scholastic, pedant, and heretic.

Dr. Bohrer was charged during the first course of lectures with being an intriguer who was inciting discord in the faculty and with having a covetous eye on the chair occupied by Drake in the faculty. Visualize, if you may, the dramatic scene at the close of the first college year, Drake sitting as president listening to the reading of damning, politically conceived charges against him, containing recommendations for his expulsion from the faculty and on putting the question to hear a unanimous concurrence in the cabal to deprive him of all further voice in, or connection with, the destiny of the child of his fondest dreams. This repugnant act divided the thriving frontier community into two hostile camps, some of the generous endowments were withdrawn, the subject was vehemently discussed in counting house, social gathering, and home. Drake, however, possessed that rare disposition which enables men to be serene in adversity and cheerful in solitude.

Thus began what has been aptly limned by an historian as the "Thirty year war," a war which was destined to continue throughout many a weary year to the detriment of college and community.

This bad state of affairs in the faculty was communicated to the State Legislature, with much animosity, by friends of Drake. Recognizing the chief defect as being within the faculty board of trustees, the assembly appointed a new board consisting of a non-faculty personnel, but the dissensions, bickerings, and pettifogging had cast an evil shadow athwart the temple of learning which redounded to the advantage of Transylvania, the only other medical college west of the Alleghanies.

Conditions improved under the ægis of the new board, but were far from being satisfactory. A questionnaire sent by the trustees to the public with a view of determining reasons for failure to advance, brought the following significant response: "Dissension of individuals composing the faculty at different times and the want of scientific reputation in the teachers."

How different are the *mores* of the sons of Lycurgus; they will *fight* furiously as long as they are paid, but when the court hands down a decision lawyers lock arms, repair to a liquid joy dispensing emporium and proceed pleasantly to pour a few libations upon the altar and fanes of friendship. Verily it may be said of doctors what Macauley said of the Stuarts: "They learn nothing, they forget nothing." Thus the Ohio Medical College continued to muddle through until the year 1835 at which time a complete reorganization was effected. Drake was offered a chair in the new faculty but he did not accept.

The college continued to function with varying degrees of success, perhaps almost keeping abreast with mediocrity, attracting students from widely separated places.

Some outstanding men and others, by contrast, mere mental weaklings, filled or occupied the various chairs and students possessing mere rudiments of education filled the benches. Results of the 2 years' course of lectures were in some instances astounding; men graduated with high

ideals, fond hopes, and considerable learning, who were destined to carry the name of the Ohio Medical College to remote parts of the globe, doctors who later in life became highly proficient as teachers, practitioners, investigators, authors in medicine, art, and literature.

After his expulsion by the faculty-trustees in 1820, Drake taught successively at Transylvania, Louisville, and Jefferson Colleges.

While the "Thirty year war" raged with unabated fury, Drake was engaged in another war whose objective was to destroy ignorance and open the door of knowledge. In this conquest he traveled extensively on horseback and on foot, by boat and by canoe, covering practically all of the territory lying between the Alleghany and Blue Ridge mountains and the snow-capped peaks of the Rockies, from the Great Lakes to New Orleans. In his travels, Drake frequently slept with the Indians, his rest was disturbed by weird noise of forest and lagoon, his way lay through uncharted woods beset by cries of wild beasts and the war-whoops of hostile Indians. Add to such *conveniences* of travel the rigors of winter, the heat of summer, and you will have but an incomplete picture of the hardships which this intrepid student encountered.

In these laborious journeys he collected material for his monumental work, "Diseases of the Interior Valley of America," a mere mention of the various topics of which would require all of the space allotted to this thumb sketch of the Ohio Medical College. In recognition of this great work the University of Edinburgh conferred on him the honorary degree of philosophy.

Drake promulgated a plan to connect Cincinnati by canal with the Great Lakes and by rail with the South. He lived to see the former accomplished, and the Southern railway was built by the city a few years after his death. The commercial and social value of these improvements to the life and progress of Cincinnati are indisputable and incalculable.

He wrote knowingly, extensively on many topics: disease, geology, climate, astronomy, farming, forestation, rain fall, and numerous other themes. He was a walking compendium of useful information, exemplary in his habits, always the student, a man whose life and works are worthy of emulation by those who aspire to success in the realm of art, literature, medicine, or life itself.

In 1849 the Ohio Medical College was in a state of mental apathy and physical decay. Drake, now recognized as one of the foremost men of the time, was believed to be the only hope for the future of the institution and an appeal was made to him, by profession and public, to join the faculty. He accepted and began a course of lectures in November, 1849. He was received by the students with that acclaim which stimulates the mental faculties of a lecturer to put forth his best efforts to transmit ways and means for obtaining knowledge by his classes. The splendor of simplicity and elegance of diction which marked his opening address to the students are characteristic of the man he was, in this he told without rancor or animosity of his continual solicitation for the welfare of the college and his undying devotion to the child of his creation. He continued to lecture at the college until pneumonia ended his earthly career on November 6, 1852.

Two years before his death he refused to accept the presidency of the American Medical Association, saying he was not worthy of such honor.

Practically illiterate at the age of 15, Drake faced the world with a firm resolution to acquire an education. How well he achieved his objective is attested not alone by his scientific attainments but likewise by his ability to read the classics in the original and deliver lectures in Latin. He was a living example of what Buffon had in mind when he said, "Genius is unflagging patience."

He had a keen perception for his surroundings, possessed in unusual degree the powers of deduction and retention, and was interested in all things pertaining to mankind. He was born at Plainfield, New Jersey, of untutored parents, October 20, 1785. His voice is silent but the memory lingers and shall linger to challenge comparison with any American doctor so long as the written word shall record the passing of time.

In the year 1896, just 77 years after Drake founded the Ohio Medical College, the institution became, by legislative enactment, the College of Medicine of the University of Cincinnati, a municipally built, owned, and operated university, consisting of nine major colleges with a competent corps of teachers. The Kettering laboratory, Holmes Hospital, and The Cincinnati General Hospital afforded students ample opportunity for experimentation and clinical observation.

The University has an imposing group of buildings located in a beautiful campus surrounded by virgin forest; 12,000 to 13,000 students attend annually.

What lively sensations of delight would surge through the imaginative brain of him who conceived the plan, if his eyes could behold the present picture, a picture which in his vision he saw and with his pen described, now brought to full fruition by a worthy successor, Dr. Christian R. Holmes.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

WILLIAM D. HAGGARD, Nashville, *President* ROBERT B. GREENOUGH, Boston, *President-Elect*
FRANKLIN H. MARTIN, Chicago, *Director-General*
ARTHUR W. ALLEN, *Chairman;* ERNEST M. DALAND, *Secretary, Committee on Arrangements*

PROGRAM FOR THE 1934 CLINICAL CONGRESS IN BOSTON

CLINICAL CONGRESS PROGRAM IN BRIEF

Monday, October 15

9:30. Hospital conference—Copley-Plaza Ballroom.
2:00. Clinics in hospitals.
2:00. Hospital conference—Copley-Plaza Ballroom.
2:00. Surgical film exhibition—Georgian Room, Statler.
8:15. Presidential meeting—Symphony Hall.

Tuesday, October 16

9:00. Clinics in hospitals.
9:30. Hospital conference—Copley-Plaza Ballroom.
10:00. Surgical film exhibition—Georgian Room, Statler.
2:00. Clinics in hospitals.
2:00. Hospital conference—Massachusetts General Hospital.
2:00. Surgical film exhibition—Georgian Room, Statler.
2:00. Section on ophthalmology—John Hancock Hall.
2:30. Fracture conference—Copley-Plaza Ballroom.
4:00. Ether Day Celebration—Massachusetts General Hospital.
5:00. Pathological conference—Georgian Room, Statler.
8:00. Hospital conference—Georgian Room, Statler.
8:15. Scientific session—Copley-Plaza Ballroom.

Wednesday, October 17

9:00. Clinics in hospitals.
9:30. Hospital conference—Copley-Plaza Ballroom.
10:00. Surgical film exhibition—Georgian Room, Statler.
2:00. Clinics in hospitals.
2:00. Symposium: Cancer is Curable—Copley-Plaza Ballroom.
2:00. Section on otolaryngology—John Hancock Hall.
2:00. Surgical film exhibition—Georgian Room, Statler.
2:30. Hospital conferences—Boston Lying-In and St. Elizabeth's Hospitals.
5:00. Pathological conference—Georgian Room, Statler.
8:00. Community health meeting—Boston Arena.
8:15. Scientific session—Copley-Plaza Ballroom.

Thursday, October 18

9:00. Clinics in hospitals.
9:30. Hospital conference—Copley-Plaza Ballroom.
10:00. Surgical film exhibition—Georgian Room, Statler.
11:30. State and provincial executive committees—Georgian Room, Statler.
1:30. Annual meeting—Copley-Plaza Ballroom.
2:00. Clinics in hospitals.
2:00. Section on ophthalmology—John Hancock Hall.
2:30. Hospital conference—Beth Israel Hospital.
3:30. Symposium: Diseases of the Œsophagus—Copley-Plaza Ballroom.
5:00. Pathological conference—Georgian Room, Statler.
8:15. Scientific session—Copley-Plaza Ballroom.

Friday, October 19

9:00. Clinics in hospitals.
10:00. Surgical film exhibition—Georgian Room, Statler.
11:00. Meeting of new Fellows, class of 1934—Copley-Plaza Ballroom.
2:00. Clinics in hospitals.
2:00. Surgical film exhibition—Georgian Room, Statler.
2:00. Conference on industrial medicine and traumatic surgery—Copley-Plaza Ballroom.
2:00. Section on otolaryngology—John Hancock Hall.
5:00. Pathological conference—Georgian Room, Statler.
8:15. Convocation—Symphony Hall.

FOR the twenty-fourth annual Clinical Congress of the American College of Surgeons to be held in Boston, October 15–19, the surgeons of that great medical center have organized under the leadership of a strong and representative committee and have prepared a program of clinics and demonstrations that will provide a complete showing of their clinical activities in all departments of surgery. The Committee has been assured of the hearty co-operation of the clinicians at the medical schools and more than thirty hospitals that will participate in the program. The clinical program as prepared by the Committee is presented in the following pages.

It will be noted that operative clinics and demonstrations in the hospitals are scheduled for the afternoon of Monday, October 15, beginning at 2 o'clock, and for the mornings and afternoons of each of the following four days. The schedules here published are to be further revised and amplified during the weeks preceding the Congress. The real program will be published daily during the Congress—a complete and accurately detailed program—to be posted in the form of bulletins at headquarters each afternoon for the

succeeding day. The same material will be issued in printed form the following morning.

Special features of the clinical program include: (1) Cancer clinics demonstrating the treatment of cancer by surgery, radium and the X-ray; (2) fracture clinics at which modern methods in the treatment of fractures will be demonstrated; (3) clinics in traumatic surgery for the presentation of methods used in the rehabilitation of injured patients by surgery and physiotherapy.

EVENING MEETINGS

Programs for the five evening sessions, as prepared by the Central Executive Committee, are presented in the following pages. At the presidential meeting on Monday evening in Symphony Hall, the president-elect, Dr. Robert B. Greenough, of Boston, will deliver his inaugural address. A feature of this session will be the John B. Murphy oration in surgery by Dr. Donald C. Balfour, of Rochester, Minn.

A number of distinguished surgeons from abroad who will be in attendance at the Clinical Congress will be introduced at this session. Among the visiting surgeons will be the following: Dr. Bethel Solomons, Dublin, Ireland; Sir Harold Gillies, Mr. A. Lawrence Abel, and Mr. F. J. Browne, London, England; Mr. Harry Platt, Manchester, England; Dr. Alexander MacLennan, Glasgow, Scotland; Dr. Rafael Silva, Mexico City, Mexico; Prof. Josef Halban, Vienna, Austria; Dr. Hans Widenhorn, Freiburg, Germany.

On Tuesday, Wednesday, and Thursday evenings the scientific sessions will be held in the ballroom of the Copley-Plaza Hotel at which eminent surgeons of the United States and Canada together with visiting surgeons from foreign countries will present and discuss papers on surgical subjects of timely importance.

The annual Convocation of the College will be held in Symphony Hall on Friday evening on which occasion the 1934 class of candidates will be received into Fellowship in the College. The president, Dr. Robert B. Greenough of Boston, will speak on "Special Cancer Clinics," and the Fellowship address will be delivered by Dr. Lotus D. Coffman, president of the University of Minnesota.

SYMPOSIUM: CANCER IS CURABLE

Further reports by clinicians from various parts of the United States and Canada, presenting additional statistics on the cure of cancer in addition to reports presented at the 1932 and 1933 sessions of the Clinical Congress, will be included in a symposium on cancer to be presented under the auspices of the Committee on the Treatment of Malignant Diseases in the ballroom of the Copley-Plaza Hotel on Wednesday afternoon.

CHARLES A. DUKES, M.D., Oakland, Calif., presiding.
General Subject of Curability of Cancer. FRANKLIN H. MARTIN, M.D., Director-General.
General Cases of Five Year Cures. ROBERT S. CATHCART, M.D., Charleston, S. C.; ROY D. MCCLURE, M.D., and ARTHUR MCGRAW, M.D., Detroit; MONT R. REID, M.D., and WILLIAM MILLAR, M.D., Cincinnati; HARRY C. SALTZSTEIN, M.D., Detroit; THOMAS A. SHALLOW, M.D., Philadelphia; FRANCIS CARTER WOOD, M.D., and BENJAMIN RICE SHORE, M.D., New York; A. C. SCOTT, M.D., Temple, Texas.
Cancer of the Stomach and Intestines. WILLIAM T. COUGHLIN, M.D., St. Louis.
Cancer of the Pelvic Organs and Breast. FREDERICK C. HOLDEN, M.D., New York; C. JEFF MILLER, M.D., New Orleans.
Cancer of the Breast. HUBERT A. ROYSTER, M.D., Raleigh, N. C.; HUGH H. TROUT, M.D., Roanoke, Va.
Cancer of the Pelvic Organs. FREDERICK J. TAUSSIG, M.D., St. Louis.
Cancer of the Genito-Urinary Organs. EDWIN BEER, M.D., New York.
Cancer of the Rectum. A. LAWRENCE ABEL, F.R.C.S., London, England.
Cancer of the Mouth and Larynx. GORDON B. NEW, M.D., Rochester, Minn.
Lymphatic Tumors. LLOYD F. CRAVER, M.D., New York.

Following these reports a group of papers descriptive of accepted methods for the treatment of cancer will be presented as follows:

Cancer of the Stomach Treated by Surgery. J. SHELTON HORSLEY, M.D., Richmond, Va.
Cancer of the Cervix Treated by Surgery and Irradiation. GEORGE GRAY WARD, M.D., New York.
Cancer of the Breast Treated by Surgery and Irradiation. STUART W. HARRINGTON, M.D., Rochester, Minn.
Cancer of the Lip Treated by Surgery and Irradiation. ELLIS FISCHEL, M.D., St. Louis.
Cancer of the Bladder Treated by Surgery and Irradiation. WILLIAM E. LOWER, M.D., Cleveland.

FRACTURE CONFERENCE

A conference on fractures, under the auspices of the College Committee on the Treatment of Fractures, will be held in the ballroom of the Copley-Plaza Hotel on Tuesday afternoon.

Among the papers to be presented are:

One Thousand Consecutive Fractures of Both Bones of the Leg. WILLIAM SENGER, M.D., in collaboration with J. SIMS NORMAN, M.D., Pueblo, Colo.
Operative Treatment of Fractures of Long Bones. HANS WIDENHORN, M.D., Freiburg, Germany.
Treatment of Fracture of the Carpal Scaphoid. D. W. GORDON MURRAY, M.D., Toronto.
Fractures of the Jaw. ROBERT H. IVY, M.D., Philadelphia.
Acute Fractures. MELVIN S. HENDERSON, M.D., Rochester.
Colles' Fracture. HARRY PLATT, M.S., F.R.C.S., Manchester, England.
Further Observations of the Nicola Operation for Recurrent Dislocation of the Shoulder. TOUFICK NICOLA, M.D., New York.

Also, under the auspices of the same Committee, using manikins, splints, tables, and other accessory equipment, hundreds of fractures will be practically demonstrated daily as a part of the scientific exhibition at the Statler Hotel.

CONFERENCE ON INDUSTRIAL MEDICINE AND TRAUMATIC SURGERY

During the past four years the College has conducted investigations and surveys in many parts of the United States to ascertain present medical conditions in industry and to inform employers of adequate methods. The results of these surveys will be presented in the symposium to be held in the ballroom of the Copley-Plaza Hotel on Friday afternoon under the auspices of the Board on Industrial Medicine and Traumatic Surgery. Other papers in the symposium deal with the clinical aspects of injuries occurring in industry and methods of rehabilitation of the injured.

FREDERIC A. BESLEY, M.D., Chairman, Board on Industrial Medicine and Traumatic Surgery, presiding.

The Program of the American College of Surgeons in Industrial Medicine and Traumatic Surgery. FRANKLIN H. MARTIN, M.D., Chicago, Director-General.

A Four Years' Survey of Medicine and Surgery in Industry. M. N. NEWQUIST, M.D., Chicago.

The Value of an Organized Medical Service in an Industrial Establishment. HOMER L. FERGUSON, President, Newport News Shipbuilding and Dry Dock Company, Newport News, Va.

Papilloma and Carcinoma of the Bladder Among Dye Workers. GEORGE H. GEHRMANN, M.D., Medical Director, E. I. du Pont de Nemours & Company, Wilmington, Del.

Back Injuries. FREDERIC J. COTTON, M.D., Boston.

Head Injuries and Their Treatment. WALTER E. DANDY, M.D., Baltimore.

Reconstruction Surgery. SIR HAROLD GILLIES, C.B.E., F.R.C.S., London.

Infections of the Hand. ALLEN B. KANAVEL, M.D. Chicago.

COMMUNITY HEALTH MEETING

Following its established custom and in recognition of its obligation to the public to provide authoritative information on modern surgery, better hospitals, and the prevention of disease, a community health meeting will be held on Wednesday evening, October 17, under the auspices of the American College of Surgeons in connection with the Clinical Congress. For this purpose the Boston Arena, which accommodates approximately 10,000 people, has been engaged. A program appropriate for the occasion has been prepared consisting of brief interesting talks on scientific medicine, health and hospitals. These talks will be supplemented by an interesting new sound motion picture on modern hospital care.

ROBERT B. GREENOUGH, M.D., Boston; President, American College of Surgeons, presiding.

Address of Welcome. ARTHUR W. ALLEN M.D., Boston

The American College of Surgeons—Its Aims and Objects. FRANKLIN H. MARTIN, M.D., Chicago.

A Century of Progress in Medicine. ALLEN B. KANAVEL, M.D., Chicago.

The Rôle of Experimental Medicine in Human Salvage. GEORGE W. CRILE, M.D., Cleveland.

Maternal Care in Approved Hospitals. MALCOLM T. MACEACHERN, M.D., Chicago.

Cancer—Its Prevention and Control. CLARENCE COOK LITTLE, Sc.D., New York.

Cancer—Its Curability. CHARLES A. DUKES, M.D., Oakland, Calif.

The Care of the Injured. FREDERIC A. BESLEY, M.D., Waukegan, Ill.

The Ache in Your Back. PHILIP H. KREUSCHER, M.D., Chicago.

Doctors, Hospitals, and Patients. ROBERT JOLLY, Houston, Texas.

Motion Picture—"Good Hospital Care."

OPHTHALMOLOGY AND OTOLARYNGOLOGY

The committee in charge of the section on surgery of the eye, ear, nose, and throat has arranged a program of ophthalmological and otolaryngological clinics and demonstrations at the hospitals and medical schools. This appears in the following pages, and in addition programs for sessions on Tuesday, Wednesday, Thursday, and Friday afternoons in John Hancock Hall, located on St. James Avenue midway between the Statler and Copley-Plaza Hotels. At these sessions distinguished specialists will present papers on subjects of timely interest.

A symposium on "Diseases of the Œsophagus" will be presented on Thursday afternoon at 3:30 in the ballroom of the Copley-Plaza Hotel following the annual meeting. The program follows:

An X-ray Study on Lesions of the Œsophagus (statistical study with lantern slides). A. S. MACMILLAN.

Infection of the Œsophagus in Acute and Chronic Disease; Fibrosis of the Terminal Portion of the Œsophagus (Cardiospasm), Etiology and Treatment. HARRIS P. MOSHER.

The Surgical Approach to the Œsophagus. EDWARD D. CHURCHILL.

ANNUAL MEETING

The annual meeting of the College will convene in the ballroom of the Copley-Plaza Hotel at 1:30 o'clock Thursday afternoon. Reports on the activities of the College will be presented by the officers and chairmen of the standing committees, followed by the election of officers.

MEETING OF NEW FELLOWS

Candidates for Fellowship in the American College of Surgeons, class of 1934, will assemble in the grand ballroom of the Copley-Plaza Hotel at 11 a.m. on Friday for the necessary instructions previous to receiving their Fellowships.

PATHOLOGICAL CONFERENCES

The Committee has arranged for a series of pathological conferences to be held in the Georgian Room at the Statler Hotel on Tuesday, Wednesday, Thursday and Friday afternoons from 5 to 6 o'clock, when selected gross specimens from operations performed that day at various hospitals will be demonstrated, accompanied by brief discussions of the lesions involved. In certain cases immediate frozen sections will be demonstrated to correlate the gross and microscopic pathology. Prepared fresh pathological specimens will be on display daily in refrigerated cases in an adjoining room. The demonstrations will be conducted by a group of pathologists from Boston hospitals under the direction of Dr. Shields Warren, as follows:

Tuesday—S. BURT WOLBACH and G. KENNETH MALLORY
Wednesday—TRACY B. MALLORY and TIMOTHY LEARY
Thursday—CHARLES F. BRANCH and H. E. MACMAHON
Friday—SIDNEY FARBER and J. STEWART ROONEY

SURGICAL FILM EXHIBITIONS

Throughout the week surgical motion picture films, both sound and silent, will be exhibited daily in the Georgian Room of the Statler Hotel. This showing of films demonstrating clinical features of interest has met with popular acceptance in previous years. Many new films are to be shown. Detailed programs will appear in the Daily Bulletin.

A motion picture depicting approved methods of transportation of fracture cases is to be shown daily in the dome room at the Massachusetts General Hospital.

STATE AND PROVINCIAL COMMITTEES

A meeting of the State and Provincial Executive Committees with officers of the College has been called for 11:30 o'clock Thursday morning in the Georgian Room of the Statler Hotel. This meeting is called for the purpose of obtaining information on which may be based the itinerary of the College for its sectional meetings and the desirable grouping of the states and provinces.

ETHER DAY CELEBRATION

Ether Day will be celebrated at the Massachusetts General Hospital on Tuesday with special exercises at 4 p.m. in the auditorium of the Moseley building of the hospital where ether was first administered for the production of surgical anæsthesia on October 16, 1846. The motion picture entitled "The First Public Demonstration of Surgical Anæsthesia" will be shown daily in the dome room.

ANNUAL HOSPITAL CONFERENCE

A highly practical and instructive four-day program has been prepared for the seventeenth annual hospital standardization conference during the Clinical Congress in Boston. The program appears in the following pages. Administrative, economic and educational topics will be presented by leaders in the hospital field including surgeons, trustees, administrators, nurses and research workers. These addresses will be supplemented by round table conferences and demonstrations in four of Boston's leading hospitals on Tuesday, Wednesday and Thursday afternoons.

At the opening session on Monday morning distinguished leaders in medical and hospital work will address the conference, the topics to be discussed tending to focus attention on present day problems related to hospital standardization and administration. Other sessions will be devoted to a discussion of major problems of concern to all hospitals—sterilization of surgical dressings, instruments and supplies, and standards for maternal care. Both subjects are now attracting widespread interest, and it is planned to present at these sessions the latest authentic facts pertaining thereto, expecting that such discussions will lead to a definite understanding as to the best standards to be adopted. At a special session on Tuesday evening in the Georgian Room of the Statler Hotel, a comprehensive analysis of the duties and responsibilities of the hospital trustees will be presented.

During recent years there has been a notable increased interest in hospital matters aroused through economic conditions. The problem of giving the patient the best scientific service possible at the lowest cost has seriously engaged the interest of all groups. Attention will be focused on this problem during the four-day conference. Physicians, trustees, administrators, nurses and others will have an opportunity at this meeting to discuss the many problems of mutual concern.

SCIENTIFIC EXHIBITION

The Committee on Scientific Exhibits has drawn upon the abundant medical resources of Massachusetts to provide a remarkably attractive and instructive exhibit for the benefit of the Fellows. At headquarters and in the medical institutions of Boston there will be presented unusual exhibits on various phases of historical and current events in the practice of surgery and its specialties, dentistry, anatomy, pathology, public health, and anæsthesia. An exceptional feature will be an exhibition of works of art by Massachusetts physicians.

HEADQUARTERS

The Statler and Copley-Plaza Hotels will be utilized as headquarters for the Congress. At the former, the grand ballroom and adjoining assembly room together with other large rooms on the mezzanine floor have been reserved for the exclusive use of the Congress for registration and clinic ticket bureaus, bulletin boards, technical exhibition, and executive offices. A scientific exhibit, which will be arranged by the local committee, is to be installed in the balcony of the ballroom. At the Copley-Plaza Hotel the grand ballroom will be utilized for evening scientific meetings, hospital conferences, and other large gatherings daily.

TECHNICAL EXHIBITION

The technical exhibition will be located in the ballroom and adjoining assembly room at the Statler Hotel. The registration and clinic ticket desk, together with the information bureau, will be located in these rooms in which will also be found the bulletin boards on which the daily clinical programs will be posted each afternoon. The leading manufacturers of surgical instruments, electrosurgical and X-ray apparatus, operating room lights, tables, sterilizers, hospital apparatus and supplies of all kinds, ligatures, dressings, pharmaceuticals, and publishers of books will be represented in this exhibition.

SPECIAL TRAIN TO BOSTON VIA NEW YORK CENTRAL LINES

For the convenience of those living in the central and western states, who will attend the Boston meeting, arrangements have been made with the New York Central Lines to provide a special train leaving Chicago at 10 a.m. on Sunday, October 14th, arriving in Boston at 9 a.m. on Monday. The special train will be equipped with all-steel cars of latest design, including club, compartment, observation, sleeping and dining cars. No extra fare will be charged. The train will arrive at Cleveland at 5:55 p.m., making connections there with regular trains over the Big Four from Indianapolis and Cincinnati. Fellows are urged to make their reservations for the special train at the earliest possible date, making application at the office of the assistant general passenger agent of the New York Central Lines, LaSalle Street Station, Chicago.

REDUCED RAILWAY FARES

The railways of the United States and Canada have authorized reduced fares on account of the Boston session of the Clinical Congress so that the total fare for the round trip will be one and one-third the ordinary first-class one-way fare. To take advantage of the reduced rates it is necessary to pay the full one-way fare to Boston, procuring from the ticket agent when purchasing ticket, a "convention certificate," which certificate is to be presented at headquarters for the signature of the general manager of the Clinical Congress and the visé of a special agent of the railways. Upon presentation of the viséd certificate to the ticket agent in Boston not later than October 23, a ticket for the return journey by the same route as traveled to Boston may be purchased at one-third the one-way fare.

In the eastern, central, and southern states and eastern provinces of Canada tickets may be purchased between October 11 and 16; in other sections of the United States and Canada at earlier dates. The return journey must be completed within thirty days from date of sale of ticket to Boston.

The reduction in fares does not apply to Pullman fares nor to extra fares charged for passage on certain trains. Local railroad ticket agents will supply detailed information with regard to dates of sale, routes, etc. Stop-overs may be had within certain limits.

Full fare must be paid from starting point to Boston, and it is essential that a "convention certificate" be obtained from the agent when the ticket is purchased. These certificates are to be signed by the general manager of the Clinical Congress and viséd by a special railroad agent at Clinical Congress headquarters on or before October 19. No reduction in railroad fares can be secured except in compliance with the regulations outlined and within the dates specified. It is important to note that the return trip must be made by the same route as used in going to Boston, that the certificate must be viséd at headquarters during the meeting, and return ticket purchased not later than October 23.

In the western and southwestern states, including the Pacific coast states and the western provinces of Canada, the railroads have authorized the sale of round trip tickets to Chicago at very low rates on account of A Century of Progress Exposition, so that persons from the west traveling through Chicago to Boston will find it to their advantage to buy round trip tickets to Chicago at the low rates in effect on account of the Exposition. Under this plan it will be necessary to purchase tickets to Boston from Chicago taking advantage of the "convention certificate" plan outlined above. Ticket agents should be consulted with regard to special rates.

ADVANCE REGISTRATION

The hospitals and medical schools of Boston afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the result of a survey of the amphitheaters, operating rooms, and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Clinical Congress in Boston will register in advance by applying to the offices of the College at 40 East Erie Street, Chicago.

Admittance to all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will be limited to the capacity of the room in which that clinic will be given.

A registration fee of $5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

BOSTON HOTELS AND RATES

Boston hotels will provide ample facilities and there should be no difficulty in securing first-class accommodations. It is advisable, however, for those who expect to attend the Clinical Congress to reserve their accommodations as far in advance as possible. In addition to the headquarters hotels, the Statler and Copley-Plaza, there are a number of first-class hotels within walking distance of headquarters. The following list of hotels with their rates has been prepared by the local committee:

	Minimum Rates with Bath	
	Single	Double
Bellevue, 21 Beacon Street	$3.00	$5.00
Bradford, 275 Tremont Street	2.50	3.50
Braemore, 464 Commonwealth Avenue	3.00	4.00
Brunswick, 520 Boylston Street	2.50	4.00
Buckminster, 645 Beacon Street	2.00	3.50
Canterbury, 14 Charlesgate West	2.50	3.00
Charlesgate, 535 Beacon Street		4.00
Copley-Plaza, 138 St. James Avenue	4.00	6.00
Fensgate, 534 Beacon Street	2.50	3.50
Graylyn, 20 Charlesgate West		5.00
Hemenway, 91 Westland Avenue	2.50	3.50
Kenmore, 490 Commonwealth Avenue	3.00	4.50
Lenox, Exeter Street	2.50	3.50
Lincolnshire, 20 Charles Street	3.00	4.50
Manger, North Station	2.50	3.50
Parker House, 60 School Street	3.00	4.50
Puritan, 390 Commonwealth Avenue	3.50	5.00
Ritz-Carlton, 15 Arlington Street	4.00	7.00
Sheraton, 91 Bay State Road	3.00	4.00
Somerset, 400 Commonwealth Avenue	3.00	3.50
Statler, Park Square	3.50	5.00
Touraine, 62 Boylston Street	3.00	5.00
Vendome, 160 Commonwealth Avenue	2.50	4.00
Victoria, 271 Dartmouth Street	3.00	5.00
Westminster, 124 St. James Avenue	2.50	3.50

SCIENTIFIC EXHIBITS

AT HEADQUARTERS, STATLER HOTEL

FRACTURES. Demonstrating methods of treating fractures, under the auspices of the New England Fracture Committee of the American College of Surgeons.

PLASTIC SURGERY. An exhibit of models, photographs, and diagrams, illustrating the different methods employed in plastic surgery and the results.

TRAUMATIC SURGERY. Diagrams, photographs, and charts.

ORTHOPEDIC SURGERY. An exhibit of splints and other forms of orthopedic apparatus, together with charts and photographs.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH. An exhibit illustrating the activities of this department.

CANCER. An exhibit from the Palmer Memorial Hospital, Collis P. Huntington Memorial Hospital, and the Pondville State Cancer Hospital. Lantern slides, charts, and photographs illustrating cancer of the various organs of the body; the diagnosis and the results obtained by different forms of treatment. Also, an exhibit of specimens of cancer from many parts of the body.

OPHTHALMOLOGY. Charts and photographs illustrating melanotic sarcoma and other conditions of the eye. Heredity of immune reactions; hereditary blindness; pedigree of blindness.

PATHOLOGY. The specimens removed at operations from the various hospitals in the morning will be collected and placed on exhibition in artificially cooled showcases in the afternoon, in a room adjoining the Georgian Room. At 5 p.m. these specimens will be demonstrated in the Georgian Room by a projectoscope, the microscopic sections shown, and the cases discussed.

AT HOSPITALS AND MEDICAL INSTITUTIONS

HARVARD DENTAL SCHOOL. An exhibit of models, photographs, and diagrams showing the restoration of extensive defects and deformities of the face and jaws by plastic surgery and dental prosthesis, including cases of soldiers wounded in the World War.

BOSTON MEDICAL LIBRARY. Exhibit of historical books on surgery and anatomy, and surgical medals. Historical pageant illustrating the development of surgery, Wednesday, October 17, John Ware Hall, 4 p.m.; presented by the students of Tufts College Medical School under the direction of Professor B. Spector. Exhibition of works of art by Massachusetts physicians under auspices of the Physicians Art Society.

MASSACHUSETTS GENERAL HOSPITAL. Daily, at noon, an exhibit in the Ether Dome relative to the first public demonstration of ether anæsthesia including a showing of the motion picture "The First Public Demonstration of Ether Anæsthesia." Also the motion picture film, "Fractures in Transportation."

MASSACHUSETTS CHARITABLE EYE AND EAR INFIRMARY. Anatomical specimens and œsophageal instruments.

HARVARD MEDICAL SCHOOL, Warren Museum. Anatomy, anatomical specimens; pathology, pathological specimens.

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Public Meeting—ALEXANDER BEGG, Chairman; DWIGHT O'HARA, Secretary.

Clinical Bulletin—FRANK OBER, Chairman.

Ophthalmology and Otolaryngology—GEORGE L. TOBEY JR., Chairman; LYMAN RICHARDS, Secretary, Otolaryngology; THEODORE L. TERRY, Secretary, Ophthalmology.

PROGRAM FOR EVENING MEETINGS

Presidential Meeting—Monday—October 15, 8:15 p.m.

Address of Welcome: ARTHUR W. ALLEN, M.D., Boston, Chairman, Committee on Arrangements

Introduction of Foreign Guests: FRANKLIN H. MARTIN, M.D., Chicago, Director-General

Address of Retiring President: The Background of the American Surgeon. WILLIAM D. HAGGARD, M.D., Nashville, Tenn.

Inauguration of Officers

Inaugural Address: Efficient Surgical Service in the Whole Community. ROBERT B. GREENOUGH, M.D., Boston

John B. Murphy Oration in Surgery: Principles of Gastric Surgery. DONALD C. BALFOUR, M.D., Rochester, Minn.

Tuesday—October 16, 8:15 p.m.

Living Grafts of Thyroid and Parathyroid Glands. HARVEY B. STONE, M.D., Baltimore, with the collaboration of JAMES C. OWINGS, M.D., and GEORGE O. GUY, M.D., Baltimore

Endocrine Mechanisms in Certain Functional Gynecological Disorders. EMIL NOVAK, M.D., Baltimore

Fracture Oration: The Unsolved Fracture. KELLOGG SPEED, M.D., Chicago

The Giant-Cell Tumor of Bone as a Clinical Entity. HARRY PLATT, M.S., F.R.C.S., Manchester, England

Wednesday—October 17, 8:15 p.m.

Hydrocephalus and Spina Bifida. WILDER PENFIELD, M.D., Montreal

Sterility with Special Reference to Surgical Possibilities. BETHEL SOLOMONS, M.D., F.R.C.P.I., Dublin, Ireland

Diverticulosis and Diverticulitis. IRVIN ABELL, M.D., Louisville

Plastic Surgery. SIR HAROLD GILLIES, C.B.E., F.R.C.S., London, England.

Thursday—October 18, 8:15 p.m.

Symposium on Treatment of Infections:

Infections of Clean Operative Wounds. FRANK L. MELENEY, M.D., New York
Discussion: IRVING J. WALKER, M.D., Boston

Infections of the Lip and Face. FREDERICK A. COLLER, M.D., Ann Arbor, Mich.
Discussion: ELLIOTT C. CUTLER, M.D., Boston

Phagedenic Ulcer; its Recognition and Treatment. EMILE HOLMAN, M.D., San Francisco
Discussion: EDWARD D. CHURCHILL, M.D., Boston

The Repairs of Defects Resulting from Full Thickness Loss of Skin from Burns. JAMES B. BROWN, M.D., St. Louis
Discussion: V. H. KAZANJIAN, M.D., Boston

Convocation—Friday—October 19, 8:15 p.m.

Invocation. REV. CHARLES WESLEY BURNS, D.D., LL.D., Boston

Presentation of Candidates for Fellowship. FRANKLIN H. MARTIN, M.D., Chicago, Director-General

Conferring of Fellowships. The President

Conferring of Honorary Fellowships. The President

Presidential Address: Special Cancer Clinics. ROBERT B. GREENOUGH, M.D., Boston

Fellowship Address: LOTUS D. COFFMAN, Ph.D., LL.D., President, University of Minnesota

ANNUAL HOSPITAL STANDARDIZATION CONFERENCE

Monday, 9:30–12:30—Ballroom, Copley-Plaza Hotel

Chairman's Address. WILLIAM D. HAGGARD, M.D., Nashville, Tenn.

Presentation of Seventeenth Annual Hospital Standardization Report. FRANKLIN H. MARTIN, M.D., Chicago.

Guiding Fundamental Principles for Prepayment of Hospital and Medical Services. CHARLES A. DUKES, M.D., Oakland, Calif.

The Development of Periodic Prepayment Plans for Hospital Care in England. SYDNEY LAMB, Liverpool, England.

The Hospital in Retrospect and Introspect. REV. ALPHONSE M. SCHWITALLA, S.J., Ph.D., St. Louis.

Future Trends in Hospital Management and Service. BERT W. CALDWELL, M.D., Chicago.

The Proper Interpretation of Hospital Service. NEWTON E. DAVIS, D.D., Columbus, Ohio.

What the Hospital Can Do for the Younger Surgeon. WITTEN B. RUSS, M.D., San Antonio, Texas.

Principles Governing Relation of Radiologists to Hospitals, ARTHUR C. CHRISTIE, M.D., Washington, D. C.

Monday, 2:00–5:00—Ballroom, Copley-Plaza Hotel

Standards for Obstetrical Service in Hospitals.

GEORGE W. KOSMAK, M.D., New York, presiding.

A Study of Obstetric Complications in the Woman's Hospital to Establish Proper Standardization for Statistical Purposes. GEORGE GRAY WARD, M.D., BYRON H. GOFF, M.D., and ALBERT H. ALDRIDGE, M.D., New York.

Regulations and Control of Obstetrical Practices in Institutions by Nonstaff Physicians. SAMUEL A. COSGROVE, M.D., Jersey City, N.J.

Minimum Standards of the American College of Surgeons for the Care of Obstetrical Patients in General Hospitals. ROBERT A. JOHNSTON, M.D., Houston, Texas.

General discussion led by JAMES RAGLAN MILLER, M.D., Hartford, Conn.

Tuesday, 9:30–12:30—Ballroom, Copley-Plaza Hotel

Sterilization of Dressings, Instruments, and Supplies.

G. HARVEY AGNEW, M.D., Toronto, Ont., presiding.

Observations on Sterilization of Dressings with Specific Reference to Sterilizing Chamber Temperatures and Their Relation to Sterilizer Chart Temperatures and Cultures. SAMUEL R. D. HEWITT, M.D., St. John, N. B.

A Scientific Analysis of Steam in Sterilizing, Showing How Precision Methods May Be Substituted for the Indefinite Methods now in Vogue. WEEDEN B. UNDERWOOD, Erie, Pa.

The Fundamental Principles Underlying the Mechanics and Technique of Sterilization. HURLEY T. WYATT, M.S., Madison, Wis.

Checking and Controlling Postoperative Complications. HAROLD L. FOSS, M.D., Danville, Pa.

General discussion opened by CLAUDE W. MUNGER, M.D., Valhalla, N. Y.

Tuesday, 2:00–4:00—Massachusetts General Hospital

Demonstrations and round table discussions in Hospital Standardization and Administration. Conducted by GEORGE H. BIGELOW, M.D., Director, and heads of departments.

The Organization of an Anæsthesia Service. HOWARD BRADSHAW, M.D., Anæsthetist.

Social Problems of the Surgical Patient. IDA M CANNON, Chief, Social Service Department.

Experience with a Hospital for People of Moderate Means. MORGAN J. RHEES, M.D., Assistant Director.

Eight Hour Nursing. SALLY JOHNSON, R.N.. Superintendent of Nurses.

Tuesday, 8:00–10:00 p. m.—Georgian Room, Statler Hotel

Special Session for Hospital Trustees

C. P. CURTIS, Boston, presiding.

How I, as a Hospital Trustee, View my Responsibility. IDA M. CANNON, Boston.

How I, as a Hospital Trustee, Discharge my Duties. FULLER BARNES, Bristol, Conn.

How I, as a Trustee, Judge the Efficiency of our Hospital. INGERSOLL BOWDITCH, Boston.

How the Trustees of the Hospital Can Promote Public Relations. PAUL H. FESLER, Chicago.

General discussion led by JOSEPH C. DOANE, M.D., Philadelphia.

Motion Picture—"Good Hospital Care" (sound).

Wednesday, 9:30–12:30—Ballroom, Copley-Plaza Hotel

Joint Session with Association of Record Librarians of North America. JAMES T. NIX, M.D., New Orleans, presiding.

The Use of the National Nomenclature. H. B. LOGIE, M.D., New York.

Basic Training for a Record Librarian. JESSIE N. HARNED, Rochester, N. Y.

The Organization and Management of the Medical Records Department in a Sisters' Hospital. SISTER M. PATRICIA, O.S.B., B.S., Duluth, Minn.

Round table conference—problems concerned with clinical records, with special discussion of uses of clinical records. Conducted by ALLAN CRAIG, M.D., Torrington, Conn.

Wednesday, 2:30–5:00—St. Elizabeth's Hospital

Demonstrations and round table discussions in hospital standardization and administration. Conducted by REV. THOMAS J. BRENNAN, Superintendent, and heads of departments.

Obstetrical Department in a General Hospital. CHARLES J. KICKHAM, M.D., Obstetrician-in-Chief.

Care of Emergencies. CORNELIUS J. O'LEARY, M.D., Senior Interne.

Out-Patient Department—Does the general public take undue advantage of the free clinic? REV. THOMAS J. BRENNAN, Superintendent.

Securing Autopsies—Why should the hospital try to increase the number of autopsies? FRANCIS P. MCCARTHY, M.D., Pathologist.

Wednesday, 2:30–5:00—Boston Lying-In Hospital

Demonstrations and round table discussions in hospital standardization and administration. Conducted by LOUISE S. ZUTTER, Superintendent, and heads of departments.

Pre-natal Clinic. ERMINE CONZA, R.N., Director of Clinics.

Admission of Patient, Care of Patient in Labor, Delivery Room and Immediate Postpartum Care. MARTHA WALSH, R.N., Supervisor of Delivery and Operating Floor.

Care of Newborn Baby, Formula Room. A. BERNICE DENIORD, R.N., First Assistant, Training School.
Care of Premature Baby. DOROTHY SOLOMON, R.N., Supervisor of Premature Nursery.
Care of Postpartum Patient. EDITH CARPENTER, R.N., Instructor of Nurses.
Care of Isolated or Septic Patient. FLORENCE BOSTOCK, R.N., Supervisor of Septic Division.
Postpartum Clinic. FLORENCE SWANSON, R.N., Supervisor of Clinics.
Motion picture—"Around the Clock with You and Your Baby."

Thursday, 9:30–12:30—Ballroom, Copley-Plaza Hotel

Round table conference. Conducted by ROBERT JOLLY, Houston, Texas, assisted by MALCOLM T. MACEACHERN, M.D., Chicago. This will be a clearing house for all questions arising out of deliberations of previous sessions and problems in the minds of any present, in addition to a special program of fifty important hospital questions.

Thursday, 2:30–5:00—Beth Israel Hospital

Demonstrations and round table discussions in hospital standardization and administration. Conducted by CHARLES F. WILINSKY, M.D., Director, and heads of departments.
The Training of Internes in the Social Aspects of Illness. ETHEL COHEN, Director of Social Service.
Food of Hospital Patients. MANIZA MOORE, Dietitian-in-Chief.
Nursing Problems in a General Hospital. JOSEPHINE A. MULVILLE, R.N., Superintendent of Nurses.
Application of Business Principles in the Management of Hospitals. CHARLES F. WILINSKY, M.D., Director, Deputy Health Commissioner of Boston.

OPHTHALMOLOGY AND OTOLARYNGOLOGY—SCIENTIFIC SESSIONS

Tuesday—John Hancock Hall, 2—Ophthalmology

HARRY S. GRADLE, Chicago. Recent therapeutic procedures. Discussion opened by ALLEN GREENWOOD.

JONAS S. FRIEDENWALD, Baltimore. Slit lamp ophthalmoscopy. Discussion opened by J. H. WAITE.

JOHN M. WHEELER, New York. Plastic ophthalmic surgery. Discussion opened by W. B. LANCASTER.

RAFAEL SILVA, Mexico City. Subject to be announced.

Wednesday—John Hancock Hall, 2—Otolaryngology

THOMAS E. CARMODY, Denver. Congenital deformities of the face and neck. Discussion opened by V. H. KAZANJIAN.

LOUIS H. CLERF, Philadelphia. Peroral endoscopy in otolaryngological practice.

SAMUEL J. CROWE, Baltimore. Ménière's symptom complex. Discussion opened by PHILIP MELTZER.

JOHN R. PAGE, New York. Acute infections of the middle ear and mastoid.

O. JASON DIXON, Kansas City. A departure in the management of acute mastoid disease or the advantages of conservative treatment in acute mastoid disease. Discussion opened by LYMAN RICHARDS.

GEORGE M. COATES, Philadelphia. Diagnosis of chronic infection of the tonsils in relation to indications for operation in cases of chronic focal infection.

WILLIAM V. MULLIN, Cleveland. Present status of infection of the upper respiratory tract in its relation to focal infection. Discussion by H. ARCHIBALD NISSEN.

EDWARD ZEIGELMAN, San Francisco. The cellular character of one hundred temporal bones; clinical and surgical significance, lantern slides.

Thursday—John Hancock Hall, 2—Ophthalmology

LUTHER C. PETER, Philadelphia. The technique of orthoptic training in strabismus. Discussion opened by LEGRAND H. HARDY, New York.

CLARENCE KING, Cincinnati. Tuberculin in the treatment of ocular tuberculosis. Discussion opened by MERRILL KING.

WILLIAM L. BENEDICT, Rochester, Minn. Intravenous therapy in diseases of the uveal tract (salvarsan, gold sodium thiosulphate). Discussion by ALBERT H. BROWN, Cincinnati.

C. N. SPRATT, Minneapolis. Closure of the cataract incision (motion pictures). Discussion opened by F. H. VERHOEFF.

Ballroom, Copley-Plaza Hotel—3:30—Otolaryngology

A. S. MACMILLAN. An X-ray study on lesions of the œsophagus (statistical study with lantern slides).

HARRIS P. MOSHER. Infection of the œsophagus in acute and chronic disease; fibrosis of the terminal portion of the œsophagus (cardiospasm), etiology and treatment.

EDWARD D. CHURCHILL. The surgical approach to the œsophagus.

Friday—John Hancock Hall, 2—Otolaryngology

SAMUEL J. KOPETZKY, New York. Recent developments in the diagnosis of meningitis.

WELLS P. EAGLETON, Newark, N. J. Meningitis—result of disease of the petrous apex and sphenoidal basis.

MARVIN F. JONES, New York. Pathways of approach to the petrous pyramid. Discussion by HARRY P. CAHILL.

WILLIAM MITHOEFER, Cincinnati. When and how shall a nasal sinus inflammation be treated nonsurgically?

EDWARD C. SEWELL, San Francisco. Operative treatment of sinusitis, external approach. Discussion opened by CHARLES T. PORTER.

GABRIEL TUCKER, Philadelphia. Cancer of the larynx.

HENRY B. ORTON, Newark, N. J. Cancer of the laryngopharynx. Discussion opened by LEROY A. SCHALL.

PRELIMINARY CLINICAL PROGRAM

GENERAL SURGERY, GYNECOLOGY, OBSTETRICS, ORTHOPEDICS, UROLOGY, PROCTOLOGY, SURGICAL PATHOLOGY, ETC.

CHILDREN'S HOSPITAL

Monday

F. R. OBER and associates—3. Dry clinic: Fractures in children. A. H. BREWSTER: Fractures of thigh and leg. M. KATZEFF: Fractures of the arm, elbow and forearm.

Tuesday

F. R. OBER and associates—9. Orthopedic operations.

W. E. LADD—9:30. Plastic repair of harelip and cleft palate, demonstration of cases, motion picture demonstration.

THOMAS H. LANMAN—10. Acute osteomyelitis in infancy and childhood.

PATRICK J. MAHONEY—10:30. The use of various types of skin grafts in children's surgery.

HENRY HUDSON, JR.—11. Acute appendicitis in childhood; Meckel's diverticulum.

Staff—2. Operative clinic, surgery in infants and children.

Staff—2. Orthopedic clinic. A. T. LEGG: Early treatment and the prevention of deformities in poliomyelitis. F. R. OBER: Shoulder operations. J. W. SEVER: Stabilization of the ankle joint. A. T. LEGG: Abductor limp.

Wednesday

Staff—9:30. Operative clinic.

W. E. LADD—2. Congenital hypertrophic pyloric stenosis; intussusception, diagnosis and treatment.

DONALD W. MACCOLLUM—2:30. Treatment of undescended testes, end-results over a 34 year period.

THOMAS H. LANMAN—3. Chronic pulmonary suppuration, demonstration of cases.

HENRY HUDSON, JR—3:15. Empyema in childhood, its treatment.

SIDNEY FARBER—3:30. Surgical pathology of malignant tumors in infancy and childhood, followed by demonstration of pathological specimens in department of pathology.

EDWARD C. VOGT—3:45. Myeloma in children.

Thursday

F. R. OBER and associates—9. Orthopedic operations.

W. E. LADD—9:30. Intestinal atresia, diagnosis and treatment, demonstration of cases, lantern slides.

PATRICK J. MAHONEY—10. Types of tracheo-œsophageal fistulæ; differential diagnosis and operative treatment; congenital and acquired œsophageal stricture, demonstration of methods of dilatation.

W. E. LADD—10:30. Atresia of the bile ducts, diagnosis and treatment; choleductus cyst, diagnosis and treatment.

THOMAS H. LANMAN—11. Ureteral transplantation for exstrophy of the bladder, demonstration of treated cases.

Staff—2. Operative clinic, surgery in infants and children.

Staff—2. Orthopedic dry clinic. A. H. BREWSTER: Claw feet. F. H. MORRIS: Torticollis, mastoid approach. H. FITZSIMMONS: Discussion. F. R. OBER and SIDNEY FARBER: Semilunar cartilage. H. FITZSIMMONS: Osteoclasis. R. H. MORRIS: Ligamentous operation for club feet.

Friday

Staff—9. Orthopedic clinic. S. M. FITCHET: Cleidocranial dysostosis. F. R. OBER: Shelf operations. S. M. FITCHET: Flexion deformity of the hip. A. T. LEGG: Coxa plana. F. R. OBER: Sprengel's deformity. R. H. MORRIS: Knee flexion deformity.

Staff—9:30. Operative clinic, surgery in infants and children.

W. E. LADD—2. Ulcerative colitis in childhood—diagnosis and treatment; demonstration of cases, lantern slide demonstration.

TRACY PUTNAM—2:30. A new method of treatment of hydrocephalus by endoscopic electrocoagulation of the choroid plexus.

DONALD W. MACCOLLUM—2:45. Treatment of hæmangioma by endothermy, demonstration of cases.

W. E. LADD—3. Surgical significance of pyuria in infancy and childhood, demonstration of cases, lantern slide demonstration.

T. H. LANMAN—3:30. Malignant bladder tumors in childhood.

PEABODY HOME

Wednesday

F. R. OBER and associates—9. Orthopedic clinic.

PALMER MEMORIAL HOSPITAL

Tuesday

Staff—9. Treatment of malignant disease, including surgery, electrosurgery, and radium implantation, operative clinic.

Staff—2. Dry clinics. G. A. LELAND: Carcinoma of cervix. FLETCHER COLBY: Urinary tract complications from carcinoma of the cervix. L. S. MCKITTRICK: Interstitial radiation for carcinoma of the breast. R. H. DRESSER: Irradiation of the ovary in cancer of the breast. GEORGE G. SMITH: Diversion of the urinary stream. JOHN HODGSON: Relief of pain in malignant disease.

Wednesday

Staff—9. Treatment of malignant disease including surgery, electrosurgery, and radium implantation, operative clinic.

Thursday

Staff—2. Dry clinics. D. F. JONES: Surgical management of carcinoma of the rectum. L. S. MCKITTRICK: Factors favoring early diagnosis of cancer of the colon, principles of treatment. R. H. SWEET: Polyposis of the colon. SHIELDS WARREN: Pathological aspects of rectal polypi. WYMAN RICHARDSON: Blood dyscrasias after gastrectomy and short-circuiting operations on the intestinal tract.

Friday

Staff—9. Treatment of malignant disease, surgery, electrosurgery, and radium implantation, operative clinic.

BEVERLY HOSPITAL

Thursday

PEER JOHNSON and JOHN ADAMS—10. Fracture clinic.

BOSTON CITY HOSPITAL

Monday

Staff—2. Dry clinic. J. J. REGAN, S. WEISS and D. MUNRO: The eye in arteriosclerosis, hypertension and tumor. G. K. COONSE: Treatment of shock. J. RESNIK and M. RITVO: Pellegrini-Steida's disease, diagnosis and treatment. O. J. HERMANN and E. PARKER, JR.: Synovioma of knee. F. A. SLOWICK: Septic hips.

Tuesday

DAVID D. SCANNELL, SOMERS FRASER, THOMAS W. WICKHAM and JOHN A. SETH—9. General surgical dry clinic.

First surgical service—9. General surgical operative clinic. HORACE BINNEY: Thoracoplasty for unilateral phthisis; phrenicectomy for unilateral phthisis. JAMES J. HEPBURN: Repair of ventral hernia; gastric ulcer. GEORGE W. PAPEN: Chronic empyema; cholecystitis.

Fifth surgical service—2. Dry clinic. IRVING J. WALKER: Some surgical aspects of jaundice—hyperparathyroidism, end-results; repair of common duct; chondrosarcoma of humerus, end-results; carcinoma of stomach, end-result; ligation of common carotid artery, end-result. FRANCIS F. HENDERSON: Carcinoma of lung; pancreatitis, review of sixty cases. AUGUSTUS RILEY: Prostate and vesicles as foci for retroperitoneal infection; kidney resections; demonstration of cases. CHARLES C. LUND: Peripheral arterial embolism, results of operative treatment in fifteen cases. E. EVERETT O'NEIL: Breast tumors, clinical versus X-ray diagnosis. WILLIAM A. WHITE: Subject to be announced.

ROBERT M. GREEN, JOHN T. WILLIAMS, FREDERICK L. GOOD, JOSEPH P. COHEN and associates—2. Gynecological and obstetrical dry clinic: Treatment of miscarriages; puerperal sepsis; pelvic inflammation.

Wednesday

IRVING J. WALKER, FRANCIS F. HENDERSON, CHARLES C. LUND, E. EVERETT O'NEIL and WILLIAM A. WHITE—9. General surgery, operative clinic.

Bone and joint service—9. Dry clinic. OTTO J. HERMANN: Boston City Hospital bone and joint service. THOMAS H. PETERSON: Colles' fracture therapy; Soutter traction in unreduced fractures of the forearm and old shoulder dislocations. GEORGE K. COONSE: Fracture of the olecranon, new operative repair. OTTO J. HERMANN: Recurrent shoulder dislocations repaired by the Nicola method, end-results, discussion. WILLIAM F. COTTING and MARK H. ROGERS: Subdeltoid bursitis. MARK H. ROGERS: Rupture of supraspinatus tendon, discussion. JOSEPH H. SHORTELL: Spinal fracture, therapy. RUSSELL F. SULLIVAN: Spinal fusions. OTTO J. HERMANN: Compound fracture therapy. FRANK W. MARVIN: Anæsthesia in fractures.

First surgical service—2. Dry clinic. NEWTON C. BROWDER: Results of treatment of Colles' fracture; modern splinting methods in fracture therapy. JAMES J. HEPBURN: Results in treatment of peptic ulcer; giant-cell sarcoma of bone; treatment of ventral hernia. HORACE BINNEY: Methods and results in treatment of acute empyema, lung abscess, bronchiectasis, pulmonary tuberculosis. GEORGE W. PAPEN: Methods and results in treatment of chronic empyema.

Sixth surgical service—2. Dry clinic. JAMES W. SEVER: Separation of femoral epiphysis. MARK H. ROGERS: Ankylosed hips. OTTO J. HERMANN: Treatment of intracapsular fractures of neck of femur, demonstration of cases of recent fractures and ununited fractures. FREDERIC J. COTTON: Pelvic fractures. JOSEPH H. SHORTELL: Bone grafting.

ROBERT M. GREEN, JOHN B. WILLIAMS, FREDERICK L. GOOD, JOSEPH P. COHEN, and associates—9. Gynecological and obstetrical operations.

Thursday

OTTO J. HERMANN, JOSEPH H. SHORTELL, WILLIAM F. COTTING, RUSSELL F. SULLIVAN, THOMAS H. PETERSON and G. KENNETH COONSE—9. Operative bone and joint clinic. Ward rounds, demonstration of fracture apparatus, etc.

Second surgical service—9. ROBERT C. COCHRANE: Total thyroidectomy for congestive failure and angina; parathyroid tumors. WILLIAM R. MORRISON: One hundred perforated ulcers of the stomach and duodenum from the Boston City Hospital; stomach surgery, motion picture demonstration; demonstration of following cases—total removal of stomach for cancer with anastomosis of the jejunum to the œsophagus, hour-glass deformity of the stomach, cholecystgastrotomy formed by nature. THOMAS K. RICHARDS: Knee-joint pathology. JOHN J. LUCY: Recurrent intussusception caused by intestinal tumor; carcinoma of the sigmoid. RICHARD I. SMITH: Pancreatitis. HERBERT H. HOWARD: End-results of bilateral renal tuberculosis; importance of postoperative treatment of prostatectomized patient.

Fourth surgical service—2. Dry clinic. ARTHUR R. KIMPTON: Civilian gas gangrene; tetanus; use of amniotic liquid concentrate; cavernous hæmangioma of neck; catheter in common bile duct since 1926; ununited fractures. EDWARD HARDING: Demonstration of cases. JOSEPH H. BURNETT: Colles' fracture therapy. H. A. BOUVÉ: Treatment of acute traumatic abdomen.

Sixth surgical service—2. Bone and joint dry clinic. WILLIAM F. COTTING: Gonorrhœal arthritis of the knee. RUSSELL F. SULLIVAN: Hallux valgus therapy. OTTO J. HERMANN: Fractures of the os calcis therapy, discussion. JOSEPH H. SHORTELL: Bone tumors. FREDERICK W. O'BRIEN: Pre- and postoperative X-ray therapy in malignant tumors of the bone. THOMAS H. PETERSON: "Fender" fractures.

ROBERT M. GREEN, JOHN B. WILLIAMS, FREDERICK L. GOOD, JOSEPH P. COHEN and associates—9. Obstetrical and gynecological operations.

Friday

ARTHUR R. KIMPTON, ROBERT C. COCHRANE, WILLIAM R. MORRISON, STEPHEN P. MALLETT and V. H. KAZANJIAN—9. General surgery, operative clinic.

Staff—9. Gynecological and obstetrical operations.

Staff—2. Dry clinic. J. J. REGAN and W. B. CASTLE: The eye in anæmic patients. STEPHEN P. MALLETT: Fractures of the jaw. WILLIAM R. MORRISON: Visualization of arteries and veins for diagnosis and operation of aneurysm; ligation of the first part of right subclavian artery and subsequent ligation of innominate artery for arteriovenous aneurysm of internal jugular vein and subclavian artery. OTTO J. HERMANN and WILLIAM R. MORRISON: Chronic subluxation of sternal end of clavicle. STEPHEN J. MADDOCK: The Baer maggot treatment of chronic osteomyelitis.

Physiotherapy service—9. Dry clinic. JOSEPH RESNIK: Electrodiagnosis. JOSEPH RESNIK, GIRDIE W. DICKINSON, ARTHUR J. COLE, WALDO W. ROBBINS and SIDNEY M. SIMONS: Demonstration of cases and treatment.

MASSACHUSETTS GENERAL HOSPITAL

Monday

Staff—2. Dry clinic. A. W. ALLEN: Bleeding peptic ulcer. JOHN STEWART: Water balance in the surgical patient. C. M. JONES: Nutritional œdema. L. S. MCKITTRICK: Cancer of rectum. E. L. YOUNG, JR.: Cancer of colon. J. V. MEIGS and F. W. HOYT: Rupture of Graafian follicle and corpus luteum. R. H. WALLACE: Treatment of burns.

W. J. MIXTER and associates—2. Symposium on neurosurgery. W. J. MIXTER: Rupture of the intervertebral disc. J. S. HODGSON: Head injuries requiring operation. R. G. VANCE: Healing of skull fractures. T. J. PUTNAM: Injection and coagulation of the gasserian ganglion. H. R. VIETS: Significance of forced grasping in localization of brain tumor. R. H. SMITHWICK: Surgery of the splanchnic nerves. J. S. HODGSON: Treatment of pain in malignant diseases. W. J. MIXTER: Intracranial approach to the orbit; tight scalenus anticus muscle.

V. H. KAZANJIAN and E. M. DALAND—2. Plastic surgery clinic: Partial excision of keloids; reconstruction of the lip after partial or complete removal; relief of contractures from burns; treatment of X-ray burns; treatment of congenital and acquired deformities of the face and jaws including harelip and cleft palate, prognathism of the mandible and temporomandibular ankylosis; treatment of nasal deformities.

Staff—4. Obstetrical dry clinic. T. R. GOETHALS: Cancer of cervix complicating pregnancy. M. F. EADES: Gas bacillus infection in pregnancy. J. ROCK: Habitual abortion. R. S. TITUS: Diabetes and pregnancy.

Tuesday

Staff—9. Operative clinics. General surgical, neurosurgical, genito-urinary, and thyroid services.

T. W. HARMER, H. C. MARBLE and F. G. BALCH, JR.—2. Surgery of the hand. T. W. HARMER: Anatomy, laceration of tendons and nerves, burns, Dupuytren's contracture, tuberculosis, tenosynovitis and bursitis. H. C. MARBLE: Infections, technique, crushing injuries, burns, Volkmann's contracture, fractures, old traumatic contractures. F. G. BALCH, JR.: Tumors.

GEORGE W. HOLMES and associates—2. X-ray symposium. GEORGE W. HOLMES: The management of roentgen sickness—particularly its relation to operative procedures. A. O. HAMPTON: Benign and malignant gastric ulcerations. R. SCHATZKI: The diagnosis of œsophageal varices. W. C. MARTIN: The X-ray findings in acute obstructing lesions of the gastro-intestinal tract. J. SPENCER: A portable unit for making very rapid exposures in the examination of post-operative pulmonary lesions. R. G. VANCE: Some observations on old fractures of the skull. J. R. LINGLEY: The roentgen treatment of malignant hypertension. E. G. SMITH: The combined surgical and roentgenological treatment of actinomycosis.

E. D. CHURCHILL and associates—2. Surgical research laboratories, demonstration of specimens.

M. N. SMITH-PETERSEN and associates—2. Orthopedic clinic. E. F. CAVE: Tuberculosis of the spine, end-result study. M. N. SMITH-PETERSEN: Tuberculosis of the sacro-iliac joint, end-result study. J. BARR: Tuberculosis of the hip, end-result study. G. VAN GORDER: Evaluation of spinal fusion as an operation for non-tuberculous conditions. W. A. ROGERS: Analysis of mechanics involved in the treatment of compression fractures of the spine. S. ROBERTS: Slipped capital epiphysis of the femur, analysis of operative treatment. M. N. SMITH-PETERSEN: Closed reduction of the hip versus open reduction followed by internal fixation.

Wednesday

Staff—9. Operative clinics, general surgical, neurosurgical, fracture and circulatory services.

Staff—2. Dry clinic. D. KING: Postoperative pulmonary complications. H. BRADSHAW: Methods in anæsthesia. H. SPRAGUE: Surgery in cardiac patients. L. S. MCKITTRICK and R. H. MILLER: Ulcerative colitis. E. D. CHURCHILL: Cardiolysis. E. B. BENEDICT: Gastroscopy. R. H. MILLER: Osteomyelitis. N. E. FREEMAN: Hæmorrhage in relation to shock from the standpoint of activity of the sympathetic nervous system.

J. V. MEIGS, F. ALBRIGHT and associates—2. Ovarian dysfunction clinic.

G. A. LELAND and associates—2. Fracture clinic. D. F. JONES: Organization of the fracture clinic. G. A. LELAND: Common complications of the treatment of simple fractures. M. N. SMITH-PETERSEN: Critical survey of the present treatment of fractures of the neck of the femur by nailing. H. ROGERS: The use and value of moving pictures in hospital teaching. G. VANGORDER: Presentation of cases.

E. P. HAYDEN and associates—2. Proctology.

Thursday

Staff—9. Operative clinics, general and thoracic surgery

E. A. CODMAN and associates—9. Shoulder clinic. M. N. SMITH-PETERSEN: Tendinitis (periarthritis). GEORGE W. HOLMES: X-ray diagnosis. LLOYD BROWN: Posture in relation to shoulder lesions. J. H. MEANS: Shoulder symptoms in visceral disease. HENRY VIETS: Hysteria and allied conditions. J. B. AYER: Cord and vertebral lesions. W. J. MIXTER: Brachial plexus injuries. FRANK OBER: Deltoid paralysis. HENRY MARBLE: Bunnell's operation. GEORGE W. VANGORDER: Nicola's operation. PHILIP WILSON: Ruptured supraspinatus. SUMNER ROBERTS: Fractures and dislocations of the head of the humerus. JOSEPH AUB: Toxic neuritis. WALTER BAUER: Arthritis, scapulahumeral and cervical. JOHN HODGSON: Cervical rib. CHANNING SIMMONS: Tumors of the shoulder bones. ROY MABREY: Rare conditions in the shoulder. I. B. AKERSON: Pathology of the subacromial bursa. M. N. SMITH-PETERSEN: Excision versus ankylosis of shoulder. G. H. BIGELOW: Follow-up system at the Massachusetts General Hospital. General discussion.

T. B. MALLORY—12. Clinical pathological conference.

E. D. CHURCHILL, W. WHITTEMORE and associates—2. Thoracic surgery clinic.

Staff—2. Peripheral vascular clinic. A. W. ALLEN: General management of peripheral vascular disorders. L. S. MCKITTRICK: Management of peripheral vascular lesions in diabetics. R. H. SMITHWICK: Neurovascular surgery in thrombo-angiitis obliterans and vasomotor imbalance. H. H. FAXON: Present status of the conservative treatment of varicose veins. R. R. LINTON: Peripheral embolism. R. C. PRATT: Phlebitis and lymphangitis. N. FREEMAN: The pathological physiology of gangrene. R. S. LAMPSON: The effect of tobacco smoking on the rate of peripheral blood flow. J. SEARS: Lymphedema and lymphangitis. J. L. GUARDO: Out-patient treatment of varicose veins and ulcers. JAMES DAVIDSON: Demonstration of Pavaex apparatus. J. KELLEY: Podiatry in peripheral vascular lesions.

C. C. SIMMONS and associates—2. Tumor clinic; cancer symposium.

Friday

Staff—9. Operative clinics, general surgical and orthopedic services, neurological operations; plastic surgery.

Staff—2. Dry clinic. C. LYONS: Symbiotic infections. B. VINCENT and A. V. BOCK: Surgery of spleen. A. W. ALLEN: Regional ileitis. R. H. MILLER: Tuberculosis of the lymphatic system. R. LINTON: Perforation of the cecum complicating carcinoma of colon. R. H. SMITHWICK: Gall-bladder disease, correlation of operative and X-ray findings. OLIVER COPE: The role of the pituitary and other endocrine glands in carbohydrate metabolism. H. ROGERS: Pilonidal sinus.

Staff—2. Diseases of the thyroid and parathyroid. J. H. MEANS and J. LERMAN: Medical aspects of the management of exophthalmic goiter. A. W. ALLEN: Surgical aspects of the management of exophthalmic goiter. R. H. MILLER: Nodular goiter. E. L. YOUNG: Intrathoracic goiter. E. D. CHURCHILL and FULLER ALBRIGHT: The parathyroids. S. HERTZ: The role of the pituitary in thyroid syndromes.

J. D. BARNEY and associates—2. Genito-urinary surgery.

CARNEY HOSPITAL

Monday

HAROLD G. LEE—3. Operative treatment for certain types of low back pain, demonstration of cases.

R. J. HEFFERNAN—3:30. End-results following interposition for uterine prolapse.

Tuesday

LOUIS E. PHANEUF—9:30. Vaginal hysterectomy for procidentia; repair of third degree laceration of perineum.

W. R. MACAUSLAND—9:30. Arthroplasty of hip, elbow or knee.

LOUIS E. PHANEUF—2:30. End-results in cervical Cæsarean section, lantern slide demonstration.

ROGER C. GRAVES—3:15. Transurethral resection of the prostate; selection of cases, pre-operative preparation, operative technique, after-care of patient.

Wednesday

F. B. LUND, D. F. MAHONEY, A. MCK. FRASER, W. E. BROWNE and F. J. NASH—9:30. General surgical operations.

W. E. BROWNE—2:45. Demonstration of end-results following treatment for injuries of musculospiral nerve, median nerve in forearm, ulnar nerve injuries at elbow, in midforearm, at wrist.

A. LEO BRETT—3:30. Demonstration of patient following operations for relief of paralysis resulting from myeloma with destruction of tenth dorsal vertebra; moving picture demonstration of operative technique in spinal cord tumors.

Thursday

LOUIS E. PHANEUF—9:30. Hysterectomy for fibroids.

R. J. HEFFERNAN—10:30. Vaginal operation for procidentia uteri; vaginal plastic operation for lacerations.

LOUIS E. PHANEUF—2:45. Management of placenta prævia, lantern slide demonstration.

Friday

F. B. LUND, D. F. MAHONEY, A. MCK. FRASER, W. E. BROWNE and F. J. NASH—9:30. General surgical operations.

W. E. BROWNE—2:45. Demonstration of end-results following full thickness grafts for contractures in various parts of forearm and hand. Method of preparation of splints used and various types of splints used in this work.

CAMBRIDGE CITY HOSPITAL

Tuesday

H. H. GERMAIN, D. F. MAHONEY, E. J. O'BRIEN, E. D'ERRICO and E. DOWNEY—9. Dry clinic. H. H. GERMAIN: Results in surgery of the shoulder, nerve suture; partial rupture of posterior cord of brachial plexus; fascial graft for recurrent dislocation of shoulder; arthroplasty of shoulder; arthroplasty for ankylosis of temporomaxillary articulation; skin graft for extensive burns. D. F. MAHONEY: End-results in fracture of pelvis and humerus. E. J. O'BRIEN: End-results in transurethral resection of the prostate; massive diverticulum of the bladder in a child 2½ years old. E. J. O'BRIEN: X-ray films of injuries to the head and spine. B. A. GODVIN and WALDO ROBBINS: Orthopedic clinic; end-results in fracture of hip. E. D'ERRICO: Results in injection treatment of varicose veins, moving picture demonstration. E. DOWNEY: Injection treatment of hæmorrhoids, methods used and demonstration of cases.

Wednesday

H. H. GERMAIN—9. Surgical operations. Demonstration: Nussbaum operation for leg ulcer (2 cases); tumor of the parotid (2 cases).

Staff—9. Dry clinic. MAXWELL MACDONALD: Encephalography as an aid to diagnosis in cerebral lesions. F. G. MINITER and T. E. DINAN: Results of accessory sinus operations, demonstration of cases. R. D. YOUNG: Cæsarean section. F. J. LYNCH: To be announced. J. J. MURPHY: Treatment problems of burns in general hospital. J. W. ROCKETT: Oral surgery operations. ARTHUR SARGENT and WILLIAM LANNIGAN: Orthopedic and fracture clinic. F. O. O'BRIEN: Traumatic spine and head injuries, demonstration of X-ray films. J. W. ROCKETT and F. MCLEAN: Fractures of lower and upper jaw. M. SHEA: Arthroplasty of lower jaw.

E. J. O'BRIEN and L. ROCKWELL—10:30. General surgical operations.

E. D'ERRICO—2. Acute torsion of great omentum; appendicitis complicating pregnancy.

Thursday

D. F. MAHONEY—9. General surgical operations.

J. J. MURPHY—10:30. General surgical operations; problem of rupture of urethra, fracture of pelvis and fracture of femur.

F. O. O'BRIEN—11. Traumatic spine and head injuries, demonstration of X-ray films.

BOSTON LYING-IN HOSPITAL

Tuesday and Thursday

FREDERICK C. IRVING and associates—9. Obstetrical operations; demonstrations of premature nursery, X-ray department, research laboratories, and hospital wards.

FREDERICK C. IRVING and associates—2. Dry clinic: Fetal roentgenometry; anæmia in pregnancy; treatment of heart disease in pregnancy; treatment of diabetes in pregnancy; management of neglected cases of cephalopelvic disproportion; treatment of placenta prævia; separation of the symphysis pubis; kidney function tests in pregnancy; classification of the albuminuric and hypertensive conditions in pregnancy; factors which make for viability in premature infants; erythroblastosis fetalis; barbiturates and other analgesic drugs in labor.

ST. ELIZABETH'S HOSPITAL

Tuesday

Joseph Stanton—9. Subtotal thyroidectomy.
George Keenan—9. Hysterectomy.
Charles Kickham—9. Supravaginal hysterectomy.
E. J. O'Brien—9. Transurethral resection of prostate.
E. M. Hodgkins—10. Repair of postincisional hernia with peritoneal fascial strips, by utilizing sac.
John Spellman—10. Radical operation for cancer of tongue.
Thomas Broderick—10. Spine fusion.
Benedict Boland—11. Low transverse cervical section.
Laurence Louis—11. Total thyroidectomy.
Staff—2. Dry clinic. Charles Kickham: Series of spontaneous rupture of the uterus. Russell Sullivan: End-results of bone and joint problems. Laurence Louis: Postoperative total thyroidectomy for (a) angina pectoris, (b) congestive heart disease. Francis P. McCarthy: Frozen sections; demonstration and discussion of pathological specimens.

Wednesday

Joseph Stanton—9. Hysterectomy.
George Keenan—9. Cholecystectomy.
Russell Sullivan—9. Nicola operation for recurrence of dislocation of shoulder.
Laurence Louis—9. Radical operation for cancer of the breast.
E. J. O'Brien—10. Nephrectomy for tuberculous kidney.
William McDonald—10. Operation for correction of childbirth injury.
Thomas Broderick—10. Reconstruction of hip joint.
M. McGarty—10. Removal of cartilage from knee joint.
Edward Hodgkins—11. Repair of recurrent inguinal hernia with fascial strips.
Martin Spellman—11. Sacro-iliac arthrodesis.
Staff—2. Dry clinic. William Dolan: Industrial surgery. John Whoriskey: Diseases of the gall bladder, medical cases either refusing operation or being surgically unfit, demonstration of cases. Frank Jantzen: Cholecystitis and liver dysfunction (a) with hypopituitary syndrome, (b) with hypothyroid syndrome. Michael McGarty: Flap graft in reconstruction of foot. John Casey: Disease of spleen from a surgical standpoint. Thomas Broderick: Demonstration of spinal cases with operative technique, lantern slides.

Thursday

Joseph Stanton—9. Gastro-enterostomy.
Bryant Wetherell—9. Nephrectomy.
Frank Jantzen—9. Inguinal herniotomy under local anæsthesia.
Edward Hodgkins—9. Gastro-enterostomy.
Thomas Broderick—10. Reconstruction of hip joint.
Charles Kickham—10. Prolapsed uterus with perineal repair and suspension.
William Donovan—10. Suprapubic prostatectomy.
Edward O'Brien—10. Suprapubic cystostomy.
Michael McGarty—11. Fascial repair of double recurrent inguinal hernia.
Benedict Boland—11. Tubal plastic for sterility.
Staff—2. Dry clinic. William O'Halloran: Medicine from a pre-operative and postoperative standpoint. Bryant Wetherell: Discussion of diagnosis of carcinoma of bladder. William McDonald: Polyneuritis in pregnancy. James Lynch: Vulval phlebitis complicating pregnancy, antenatal. Joseph Stanton: Hypocalcemia of unusual origin, gastric ulcer; demonstration of interesting clinical cases.

BOSTON DISPENSARY

Tuesday

Tumor clinic staff—9. Dry clinic. Frank W. Marvin: Anæsthesia in operative cases. Charles M. Proctor: Precancerous and benign lesions of the oral cavity. Charles E. Dumas: Radium technique in malignancy of the throat. Leroy A. Schall: Treatment of cancer of tonsil. George S. Speare: Malignant degeneration of sebaceous cysts. Louis E. Phaneuf: Precancerous lesions and cancer of the cervix, lantern slide demonstration. Alice Ettinger: Early diagnosis of malignancy of gastro-intestinal tract by relief method. Harold A. Chamberlin: Papillary tumors of the kidney pelvis. Roger C. Graves: Management of cancer of penis with particular reference to a modified operation for advanced cases. Myron J. Hahn: Cancer of the prostatic capsule. Isadore Olef: Management of malignancy of the lymphatic system. Hilbert F. Day: Cancer of breast, end-results. Joel Rosenberg: Bleeding carcinoma of breast without tumor. William M. Shedden: Management of cancer of rectum with particular reference to irradiation. Harold McMahon: Relation of pathology department to tumor clinic.

Wednesday

Staff—10. Dry clinic. Oliver G. Tinkham: Clinical teaching of third year medical students. Francis P. Barnum: Use of adhesive plaster. P. A. Consales: Adenomatous changes in aberrant thyroid. Hilbert F. Day: Management of a varicose vein clinic, where over 150 treatments a week are given. Edward T. Whitney: Varicose ulcers, demonstration of cases and treatment. Walter S. Levenson: High ligation of varicose veins. William M. Santoro: Injection treatment of varicoceles. S. Seymour Horlick: Results of multiple injections of varicose veins at same visit. Hilbert F. Day: Results of excision of sloughs following injection treatment.

Thursday

Staff—9. Dry clinic. John D. Adams: Shueller-Christian disease (xanthomatosis); bone tumors. Roy E. Mabrey: Chordoma and chondrosarcoma. William A. Hinton: Detection of syphilis as an aid in practice of surgery. Francis M. Thurmon: Syphilis and the differential diagnosis of surgical conditions. Joseph Skirball: Ophthalmic studies in syphilis. Grace E. Rochford: An unusual gynecological condition. Louis A. O. Goddu: Pain in the shoulder girdle. Robert W. Buck: Kidney function; renal function tests. William E. Davis: Some observations in treatment of peptic ulcer in out-patient clinic. Alice Ettinger: Diagnosis of activity of duodenal ulcer by X-ray. Katherine S. Andrews: Hiatus hernias. Hilbert F. Day: Solitary gall-stone pain relieved by posture. Demonstration of interesting X-ray plates of peptic ulcer and gall-bladder disease.

LAKEVILLE SANATORIUM

Wednesday

Z. B. Adams—9:30. Ankylosis of hip, operative. Ward rounds.
Staff—2. Dry clinic: Tuberculosis of lymph nodes, genito-urinary tract, eye, gastro-intestinal tract, peritoneum, and skin.
Z. B. Adams—2. Orthopedic dry clinic.

BETH ISRAEL HOSPITAL

Monday

Staff—2:30. Dry clinic. JOHN SEARS: Prophylactic vein ligation against embolism from phlebitis of the internal saphenous vein. MAXWELL BLOOMBERG: The prevention of scar tissue by the use of baudruche, experimental and clinical experiences, demonstration of cases. WALTER S. LEVENSON: Intraperitoneal adhesions. A. LOUIS HERMANSON: Transfusions during active bleeding from peptic ulcer. AARON THURMAN: Surgical treatment of cholecystitis. JOSEPH MEZER: Subacute pancreatitis. BORIS RAPAPORT: Comparison of postoperative complications following spinal and general anæsthesia.

Tuesday

Staff—9. Symposium on total thyroidectomy for chronic heart disease and angina pectoris. HERRMAN L. BLUMGART: Rationale of total thyroidectomy in chronic heart disease. JOSEPH RISEMAN: End-results of total thyroidectomy in angina pectoris. DAVID DAVIS: End-results of total thyroidectomy in congestive heart failure. HERRMAN L. BLUMGART: Indications and contra-indications for surgery, selection of cases. CHARLES G. MIXTER: General surgical considerations in total thyroidectomy. DAVID D. BERLIN. Technical considerations in total thyroidectomy. DAVID DAVIS: Treatment of postoperative complications. DOROTHY GILLIGAN: Parathyroid insufficiency following total ablation of the thyroid gland. MARK ALTSCHULE and ALFRED WEINSTEIN: Total thyroidectomy, moving picture demonstration; demonstration of cases.

CHARLES G. MIXTER, DAVID D. BERLIN and associates—2. Total thyroidectomy.

Wednesday

E. GRANVILLE CRABTREE and associates—9. Dry clinic, symposium on the female bladder: Demonstration of various factors related to function in health, pregnancy and disease; the use of urethrogram and cystogram in the diagnosis of bladder displacements and deformities in the multiparous woman, results of routine surgery in such cases; treatment of infections in the abnormal bladder.

W. JASON MIXTER—9. Craniotomy.

Staff—2. Dry clinic. CARL BEARSE: Acute appendicitis beyond the age of fifty. W. JASON MIXTER: Subject to be announced. ARNOLD STARR: Effect of diaphragmatic paralysis on the efficiency of cough. JACOB FINE: Postoperative distention, an experimental study. LOUIS NASON: Gas bacillus infection complicating laparotomy. BENJAMIN BANKS: Differential diagnosis of jaundice. I. R. JANKELSON: Indications for ileostomy in ulcerative colitis. CHARLES G. MIXTER: Regional ileitis. MAURICE BARRON: Is radical resection for carcinoma of the rectum the best procedure?

Thursday

Staff—9. Symposium on total thyroidectomy for chronic heart disease and angina pectoris. HERRMAN L. BLUMGART: Rationale of total thyroidectomy in chronic heart disease. JOSEPH RISEMAN: End-results of total thyroidectomy in angina pectoris. DAVID DAVIS: End-results of total thyroidectomy in congestive heart failure. HERRMAN L. BLUMGART: Indications and contra-indications for surgery, selection of cases. CHARLES G. MIXTER: General surgical considerations in total thyroidectomy. DAVID D. BERLIN: Technical considerations in total thyroidectomy. DAVID DAVIS: The treatment of postoperative complications. DOROTHY GILLIGAN: Parathyroid insufficiency following total ablation of the thyroid gland. MARK ALTSCHULE and ALFRED WEINSTEIN: Total thyroidectomy, moving picture demonstration.

CHARLES G. MIXTER, DAVID D. BERLIN and associates—2. Total thyroidectomy.

E. GRANVILLE CRABTREE and associates—2. Bladder surgery, operative and dry clinic.

Friday

MARK ROGERS and associates—9. Orthopedic dry clinic: Methods and results of manipulation of subdeltoid bursitis; slipping epiphysis, femoral neck; club foot, demonstration of application of plaster cast; method of drainage of septic knees, posterior incision; stenosing tenovaginitis, operative results; Nicola operation, end-results in three cases of recurrent dislocation of the shoulder; marble bones, repeated fracture of the femur; fractures of the long bones in Paget's disease; compression fractures of the spine in diabetes and old age; correction of hallux valgus, temporary paralysis of the sensory nerve affecting the joint.

CHARLES G. MIXTER and associates—9. General surgical operations.

Staff—10:30. Dry clinic. WILLIAM DAMESHEK: Blood changes in surgical conditions. HYMAN MORRISON: Nonsurgical simulating acute surgical disease. HARRY DEROW: Significance of postoperative rise in nonprotein nitrogen. ARNOLD STARR and S. RICHARD MUELLNER: Postoperative renal suppression. CHARLES G. MIXTER: Surgery of the large intestine. S. GARGILL and M. FALCON-LESSES: Thyroid clinic experiences.

E. GRANVILLE CRABTREE and associates—2. Renal surgery.

Staff—2. Symposium on tumors. WILLIAM DAMESHEK: Malignancies of the blood forming organs. HARRY F. FRIEDMAN and LOUIS M. FREEDMAN: Laryngeal carcinoma, diagnosis and treatment, presentation of cases. REUBEN B. DAVIDOFF: Differential diagnosis of breast tumors. CHARLES G. MIXTER: Surgical treatment of breast tumors. HARRY F. FRIEDMAN: Radiation treatment of breast tumors. MONROE J. SCHLESINGER: The diagnosis of malignancy from ascitic and pleural fluids. HARRY F. FRIEDMAN and LOUIS ALBERT: Policy toward married women in regard to carcinoma of the uterine cervix. JACOB H. SCHWARTZ: Diagnosis of carcinoma of the skin. HARRY F. FRIEDMAN: Cinema of radium treatment of carcinoma of skin. SAMUEL A. ROBINS: Roentgen diagnosis of renal tumors. E. GRANVILLE CRABTREE: Surgery in renal tumors. GEORGE C. PRATHER: Results of surgery in renal tumors; testicular tumors.

Daily Exhibit in Medical Research Laboratories.

WILLIAM DAMESHEK: Blood changes in surgical conditions. HERRMAN L. BLUMGART: Total thyroidectomy for chronic heart disease. HARRY A. DEROW: Renal function tests in surgery. SAMUEL A. ROBINS: Demonstration of interesting or unusual X-ray films. MONROE J. SCHLESINGER: Surgical pathological specimens.

SYMMES ARLINGTON HOSPITAL

Tuesday

F. J. COTTON—9. Bone and joint surgery.

A. L. BRETT—9. Tumor of the spinal cord; shoulder arthrodesis.

G. P. TOWLE—9. General surgery.

S. G. JONES—9. Volkmann's paralysis.

HARVARD MEDICAL SCHOOL

Monday

G. KENNETH COONSE and OTTO AUFRANC—2. (Bldg. C). Demonstration of the mechanical factors controlling the pulmonary circulation.

CHARLES L. SCUDDER and associates—2. (Bldg. E). Conference on fractures of the neck of the femur. A. W. REGGIO: Results of nonoperative treatment up to 1934, lantern slide demonstration. RALPH LEONARD: Roentgenological considerations; the lateral view. ROBERT VANCE: Roentgenological findings. JOSEPH FAY, HENRY MARBLE, JOHN ADAMS and OTTO HERMANN: Reports of cases treated with aid of lateral view. M. N. SMITH-PETERSEN: Operative treatment with results, moving picture demonstration. JOHN O'MEARA: Operative treatment, results; lantern slides.

Tuesday

Building D—2

GEORGE B. WISLOCKI. Studies in mammalian reproduction.

VALY MENKIN. Some problems of inflammation related to surgery.

HENRY G. SCHWARTZ. An experimental study of sympathetic reflexes.

J. L. BREMER. The postnatal growth of the mammalian lung.

HAROLD L. WEATHERFORD. The finer changes in the liver cells in anaphylactic shock.

LESTER S. KING. Some aspects of the hæmato-encephalic barrier.

Building E—2

G. A. BENNETT and WALTER BAUER. Joint changes resulting from trauma.

HUGH K. WARD. Streptococcal infections.

CECIL K. DRINKER. The physiology of the lymphatic system and its bearing on certain problems in surgery.

Wednesday

Building C—2

HALLOWELL DAVIS. Effect of cerebral anæmia on the electrical response of the cortex.

M. I. GREGERSEN. The use of hypertonic sucrose solution to reduce cerebrospinal fluid pressure without a secondary rise.

WALTER B. CANNON. Some relations of the sympathetic nervous system to surgery.

Building B—2

DAVID CHEEVER. Surgical anatomy of the abdomen, demonstrations on cadaver.

Building E—2

FRANK OBER and associates. Orthopedic problems from Children's Hospital. A. H. BREWSTER: Scoliosis. J. KUHNS: Posture and postural scoliosis. H. FITZ-SIMMONS: Congenital deformities. P. NORTON: Posterior transplants.

Thursday

TIMOTHY LEARY, DONALD MUNRO, W. J. MIXTER, J. S. BARR and WILLIAM A. ROGERS—2. (Bldg. E). Conference on trauma to the head and spine.

Friday

Symposium on Industrial Surgery—2—Building C

W. A. ROGERS. Injuries of the back.

HENRY MARBLE, F. J. COTTON and J. D. ADAMS. Injuries of the nervous system.

F. J. COTTON. Colles' fracture.

J. H. BURNETT. Carpal fractures.

Orthopedic Clinic—2—Building E

J. W. SEVER. Obstetrical paralysis.

W. GREEN. Osteomyelitis in infants and children.

R. H. MORRIS. Septic hips with involved heads.

A. T. LEGG. Osteomyelitis of the tarsus.

R. JOPLIN. Intervertebral disc—embryology, anatomy, physiology and pathology.

A. H. BREWSTER. Peroneal spasm.

R. H. MORRIS. Septic hips with involved femoral heads.

Daily

Warren Museum—M. Canavan, Curator—2

Demonstration of Dwight collection of spines illustrating deformities, anomalies, diseases. Bone tumors, with X-rays, histories, and microscopic slides, with microscopes available for examination (some of these specimens were used in the illustrations in the monograph on "Bone Sarcoma" issued by the American College of Surgeons). Models showing various types of club feet and effects of operation. Pictures illustrating pathological conditions of bone in Dr. Nichols' collection. Fractures and dislocations of bones as they existed before industrial plants provided so many safeguards. Tuberculosis of bones and joints. Syphilis of bones. Dislocation of ends of bones. Old surgical instruments, obstetrical forceps, turnkeys for extracting teeth, urological tools, cupping and leeching instruments.

MASSACHUSETTS MEMORIAL HOSPITALS

Monday

Staff—2. Dry clinic. GEORGE LEVENE: Demonstration of mechanical heart. WILLIAM D. REED: Discussion of certain oscillograms in connection with cardiac disease. LEE MACPHEE: Liver function after cholecystitis. DR. DRURY: Report on some audiograms done in brain tumor cases, before and after operation. JAMES J. JANNEY: Water metabolism. ALLEN ROWE: Subject to be announced. SAMUEL R. MEAKER: Investigation and treatment of the sterile mating.

Tuesday

Staff—2. Dry clinic. MILO C. GREEN: Resection of the ascending colon. CLIFFORD HARVEY: Gall-bladder disease in children. W. K. S. THOMAS: Abdominal surgery. CHARLES SZIKLAS: Subject to be announced. FRANK BARTON: Thyroid treatment. LOUIS G. HOWARD: Fracture of the hip.

Daily

Staff—9. Operative clinics.

CHELSEA MEMORIAL HOSPITAL

Thursday

Staff—9. Dry clinic. CHARLES P. SHELDON: Septic abortions. LLEWELLYN H. ROCKWELL: Perforated duodenal ulcer. GEORGE A. MARKS: Acute appendicitis with peritonitis. SYLVESTER B. KELLEY: Causes of death in prostatitis.

Staff—2. General surgical operations.

Staff—2. Dry clinic. GORDON MORRISON: Abdominal trauma. STEPHEN G. JONES: Volkmann's contracture. ALEXANDER P. AITKEN: Epiphyseal separation of the radius. JOHN S. HODGSON: Fractures of the skull. Discussion by FREDERICK J. COTTON.

NEW ENGLAND DEACONESS HOSPITAL

Tuesday

F. H. LAHEY, H. M. CLUTE, R. B. CATTELL and R. H. OVERHOLT—9. General surgical operations.
GILBERT HORRAX and JAMES POPPEN—9. Neurosurgical operations.
RICHARD H. OVERHOLT—9. Thoracic surgery operations.
G. E. HAGGART—9. Orthopedic operations.
JAMES B. HICKS—9. Urological operations.
LINCOLN F. SISE, PHILIP E. WOODBRIDGE and URBAN EVERSOLE—9. Anæsthesia.
F. H. LAHEY—9. Œsophageal diverticulum, dry clinic.
GILBERT HORRAX—9. Malignant exophthalmos, dry clinic.
Staff—2. Dry clinics. H. M. CLUTE: Management of obstructive jaundice; exploration of common duct. GILBERT HORRAX: Brain tumors; malignant exophthalmos. SARA M. JORDAN: Gastric cancer and ulcer; gastrojejunal ulcer. F. H. LAHEY: Total gastrectomy for cancer; gastrojejunal colic fistula; surgery of intractable ulcer. EVERETT KIEFER: Hæmorrhage in peptic ulcer. RICHARD B. CATTELL: Embolectomy; parathyroid tetany.

Wednesday

F. H. LAHEY, H. M. CLUTE, R. B. CATTELL and R. H. OVERHOLT—9. General surgical operations.
GILBERT HORRAX and JAMES POPPEN—9. Neurosurgical operations.
RICHARD H. OVERHOLT—9. Thoracic surgery operations.
G. E. HAGGART—9. Orthopedic operations.
JAMES B. HICKS—9. Urological operations.
LINCOLN F. SISE, PHILIP D. WOODBRIDGE and URBAN EVERSOLE—9. Anæsthesia.
Staff—2. Dry clinics. G. E. HAGGART: Subdeltoid bursitis; treatment of flexion deformities. JAMES L. POPPEN: End-results in trigeminal neuralgia; spinal fluid pressure dynamics. FRANK H. LAHEY: Œsophageal diverticulum; hyperthyroidism. H. M. CLUTE: End-results in hyperthyroidism. LEWIS M. HURXTHAL: Thyrocardiac patients. EVERETT KIEFER: Ulcerative colitis. RICHARD B. CATTELL: Surgical treatment of ulcerative colitis. RICHARD OVERHOLT: Limited thoracoplasty in pulmonary tuberculosis; cancer of lung.

Thursday

E. P. JOSLIN, H. F. ROOT, L. S. MCKITTRICK and T. C. PRATT—9. Surgical and medical diabetic ward rounds.
T. C. PRATT—10:30. Thigh amputation for diabetic gangrene.
L. S. MCKITTRICK—10:30. Gritti-Stokes amputation for diabetic gangrene.
Staff—2. Dry clinic: Surgery in diabetes mellitus. E. P. JOSLIN: Medical care of the surgical patient. L. RICHARDS: Otolaryngological aspect of diabetes. H. F. ROOT: Preventive measures in gangrene and infection of the lower extremities. L. S. MCKITTRICK: Factors influencing the level of amputation. T. C. PRATT: Indications for guillotine amputation. R. S. TITUS: Obstetrics in diabetes. MARK ROGERS: Depressed fracture of the spine in diabetes; subdeltoid bursitis in diabetes mellitus.

Friday

F. H. LAHEY, H. M. CLUTE, R. B. CATTELL and R. H. OVERHOLT—9. General surgical operations.
GILBERT HORRAX and JAMES POPPEN—9. Neurosurgical operations.
RICHARD H. OVERHOLT—9. Thoracic surgery operations.
G. E. HAGGART—9. Orthopedic operations.
JAMES B. HICKS—9. Urological operations.
LINCOLN F. SISE, PHILIP D. WOODBRIDGE and URBAN EVERSOLE—9. Anæsthesia.
Staff—2. Dry clinics. R. B. CATTELL: Cancer of the colon and rectum. GILBERT HORRAX: Root resection for trigeminal neuralgia; cordotomy for pain. JAMES POPPEN: Spinal cord tumors. RICHARD OVERHOLT: Cancer of the breast. JAMES B. HICKS: Transurethral resection of the prostate. H. M. CLUTE: Subphrenic abscess. F. H. LAHEY and FRANK N. ALLAN: Parathyroid tumors. J. H. WAITE: Cataract surgery in diabetes mellitus.

PETER BENT BRIGHAM HOSPITAL

Monday

DAVID CHEEVER—2. Surgical clinic.
H. F. NEWTON—3. Thoracoplasty.
S. A. LEVINE—3:30. Circulatory emergencies in surgical patients.

Tuesday

Staff—9. General surgery, operative clinic.
E. C. CUTLER—2. Total thyroidectomy.
C. L. DERICK—3. Symptoms and diagnosis of vascular thrombosis.
JOHN HOMANS—3:30. Swollen legs.

Wednesday

Staff—9. General surgery, operative clinic.
HENRY A. CHRISTIAN—2. Medical clinic.
M. C. SOSMAN—3. Recent developments in diagnostic radiology.
E. S. EMERY, JR.—3:30. Results of surgical procedures for relief of peptic ulcer.

Thursday

Staff—9. General surgery, operative clinic.
W. C. QUINBY—2. Indications for and results of total cystectomy.
J. C. ECKELS and G. P. GRABFIELD—2:30. Denervated kidney, studied by means of the divided bladder.
M. S. STROCK—3. Methods of fixation of fractures of the jaw.
S. B. WOLBACH—3.30. Surgical pathology.

Friday

Staff—9. General surgery, operative clinic.
DAVID CHEEVER—2. Cancer of the stomach.
F. C. NEWTON—2:30. Cancer of the rectum.
R. FITZ—3. Function of the spleen.
W. P. MURPHY—3:30. Treatment of pernicious anæmia, motion picture demonstration.
F. R. OBER—3:45. Treatment of neuromuscular sequelæ of pernicious anæmia.

INDUSTRIAL SURGERY

Tuesday

H. C. MARBLE and H. P. TOWLE (142 Berkeley Street)—9.
D. L. LYNCH and B. A. GODVIN (245 State Street)—9.

Wednesday

G. W. MORSE (31 St. James Avenue)—9.

Thursday

WILLIAM DOLAN (110 Milk Street)—9.

Friday

J. H. SHORTELL (260 Tremont Street)—9.
D. L. LYNCH and B. A. GODVIN (245 State Street)—9.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

Tuesday

LETITIA D. ADAMS, BLANCHE ATWOOD AND GRACE ROCHFORD—9. Surgical operations.

Staff—2. Dry clinics. GRACE ROCHFORD and MARJORIE WOODMAN: Dr. Alonzo Paine's method of delivering posterior positions, motion picture and manikin demonstration. ILIA GALLIANI: Carcinoma fundus in a young woman treated for amenorrhœa with Antuitrin S. ANSTIS MANTON: Fibrosarcoma of liver in child of six. FELICIA BANAS: Carcinoma of kidney with metastases in child of three. MIRIAM KATZEFF: Familial muscular dystrophy, demonstration of cases and motion pictures. BLANCHE ATWOOD: Demonstration of an unusual type of fracture of pelvis with special apparatus used. OLGA C. LEARY: Unusual pathological specimens with case histories.

Wednesday

LETITIA D. ADAMS, BLANCHE ATWOOD and GRACE ROCHFORD—9. Surgical operations.

MARJORIE WOODMAN, DR. FRIEDMAN, R. A. DRAPER, DR. GIBSON, E. A. POLCARI and M. K. MATARAZZO—9. Obstetrical clinic: Demonstration of analgesia, maternity ward rounds, prenatal clinics, parent-teaching clinics.

Thursday

LETITIA D. ADAMS, BLANCHE ATWOOD and GRACE ROCHFORD—9. Surgical operations.

Friday

LETITIA D. ADAMS, BLANCHE ATWOOD and GRACE ROCHFORD—9. Surgical operations.

CAMBRIDGE HOSPITAL

Tuesday

Staff—9. General surgical operations.

Staff—9. Dry clinic. A. W. DUDLEY: Subject to be announced. H. F. DAY, E. H. MCMAHON and H. P. STEVENS: Lipoid degeneration of uterus. SOMERS FRAZER: Subject to be announced. DAVID ROSE: Subject to be announced. C. T. O'CONNOR: Cæsarean section. H. L. SEVER: Delivery of a living child from dead mother. E. H. MCMAHON: Pathological subject to be announced. T. H. LANMAN, P. J. MAHONEY and J. W. NICHOLS: Subject to be announced. W. STEWART WHITTEMORE: Subject to be announced.

Staff—2. Dry clinic. A. H. CROSBIE and H. A. CHAMBERLAIN: Horseshoe kidney. H. F. DAY: Effect of posture on the solitary gallstone. S. S. HANFLIG: Osteomyelitis. STANLEY NOWAK: Subject to be announced. OSCAR RAEDER: Subject to be announced. H. P. STEVENS: Analysis of cases of biliary surgery.

LONG ISLAND HOSPITAL

Wednesday

R. H. MORRIS and T. H. PETERSON—9. Fracture clinic: Fracture of the neck of the femur in elderly people; demonstration of Soutter traction apparatus.

H. R. VIETS—9. Neurosurgical diagnosis.

J. H. CUNNINGHAM and C. S. SWAN—9. Urological operations.

A. S. MACMILLAN—2. X-ray demonstration.

I. B. AKERSON—2. Pathological demonstration.

C. L. SWAN, R. I. SMITH and T. C. PRATT—2. General surgical operations.

NEWTON HOSPITAL

Tuesday

E. D. LEONARD—9. Breast amputation.

G. M. MORRISON—9. Reconstruction of elbow.

G. K. COONSE—9. Operation for fractured patellæ.

E. G. CRABTREE—9. Cystotomy.

F. W. MARVIN—9. Pantocain anæsthesia.

D. G. NUTTER—9:15. Desmoid cysts of the abdomen.

R. I. SMITH—9:30. Carcinoma of the duodenum.

G. C. PRATHER—9:30. Renal calculus.

N. P. BRACKETT—10. Strangulated hernia in the aged.

D. G. NUTTER—10. Hysterectomy for fibroids.

G. K. COONSE—10. Triceps repair of olecranon fracture.

G. M. MORRISON—10. Ankle fractures.

F. R. CLARK—10. Cæsarean section.

H. WATTERS—10:15. Intussusception in infancy.

D. G. WILCOX—10:30. Pyosalpinx.

E. D. LEONARD—10:45. Paralytic ileus.

R. I. SMITH—11. Complete thyroidectomy for angina pectoris.

N. P. BRACKETT—11. Cholecystectomy.

H. G. DUNPHY—11. Ligation of saphenous vein for varicose ulcer.

Fracture and orthopedic services—9. Dry clinic: Demonstration of application of plaster casts, Boehler technique; application of Anderson well leg traction apparatus; treatment of fractures of the spine, including hyperextension, frames, jackets, etc.; treatment of Colles' fracture by Cotton-Loder method; demonstration of new type humeral traction abduction splint.

Staff—2. Symposium on obstetrics. E. GRANVILLE CRABTREE: Discussion of urinary tract infection in pregnancy. GEORGE C. PRATHER: Discussion of lone kidneys in pregnancy. F. R. CLARK, M. F. EADES, and G. E. MAY: Pre- and postoperative care of patients.

ROBERT G. VANCE—2. X-rays of traumatic skulls.

EVANGELINE BOOTH MATERNITY HOSPITAL

Wednesday

A. K. PAINE, H. S. FINKEL, W. J. MCDONALD, M. G. BERLIN, J. HOPKINS, D. GOLDFARB, A. A. LEVI, J. J. CONWAY, H. BAKER, S. OSGOOD and R. T. PHILLIPS—9. Gynecological operations and obstetrical procedures.

Staff—2. A review by demonstration, charts, pictures, and exhibits, of the obstetrical experience of the Booth Hospital: Maternal mortality, factors responsible for the declining rate at the Booth Hospital; the bleeding cases, statistics, management, and results; obstetrical sepsis; amnesia, analgesia, and anæsthesia in labor, results from the standpoint of safety, efficiency, effects on operative incidence, Cæsarean section, incidence, indications, and mortality; toxæmia of pregnancy, treatment, methods and results over a fourteen year period; "debunking" pelvimetry; heart disease complicated by pregnancy; fetal mortality, analysis of four hundred cases, pathology.

WALTHAM HOSPITAL

Friday

R. L. DENORMANDIE, T. W. HARMER, D. MUNRO, J. D. BARNEY, J. W. SEVER, H. Q. GALLUPE, R. COLLINS and H. A. WOOD—9. Surgical operations.

R. L. DENORMANDIE, T. W. HARMER, D. MUNRO, J. D. BARNEY, J. W. SEVER, H. Q. GALLUPE, R. COLLINS and H. A. WOOD—2. Dry clinics: General surgery, orthopedics, obstetrics, pathology, etc.

FAULKNER HOSPITAL

Wednesday

F. J. COTTON, E. G. BRACKETT and associates—9. Bone and joint clinic, operative and dry.

Staff—2. Dry clinic. E. G. BRACKETT: Lame back. F. J. COTTON: Bone tumors; fractures of pelvis. H. C. MARBLE: Hand surgery; fractures of the forearm. J. D. ADAMS: Traumatic knees. WILLIAM A. ROGERS: Compression fracture of spine. E. A. CODMAN: Shoulder lesions. B. A. GODVIN: Os calcis fractures. W. F. COTTING: Ankle fractures. H. K. SOWLES: Elbow fractures. Demonstration of X-ray plates and pathological specimens. G. L. DOHERTY: Arm fractures. J. F. GIBBONS: Case of multiple fractures.

Thursday

E. L. YOUNG, JR., R. C. COCHRANE, A. R. KIMPTON and associates—9. Operative clinic.

J. R. TORBERT and R. S. TITUS—11. Obstetrical clinic.

S. W. WIGGIN—11. Postoperative pulmonary complications.

Staff—2. Symposium on pre-operative immunization of the peritoneal cavity: H. L. JOHNSON: Theoretical and experimental evidence of the benefit of amfetin. E. L. YOUNG, JR. and EVERETT O'NEIL: Clinical evidence of immunity from amfetin injection. R. C. COCHRANE and BURTON HAMILTON: Total thyroidectomy for heart disease. F. G. BALCH, JR.: Injection treatment of hæmorrhoids.

COLLIS P. HUNTINGTON MEMORIAL HOSPITAL

Monday

Staff—2:15. Tumors and diseases of bones, dry clinic. J. C. AUB: Calcium metabolism in diseases of the bones. CHANNING C. SIMMONS: Malignant tumors of bone. RICHARD DRESSER: Radiological diagnosis of bone tumors and certain rare forms of skeletal diseases. C. C. FRANSEEN: The phosphatase content of the blood in bone tumors and skeletal diseases.

GEORGE A. LELAND and J. V. MEIGS—3:30. Carcinoma of the cervix.

Friday

Staff—2:15. Carcinoma of the oral mucous membrane, dry clinic. CHANNING C. SIMMONS: Choice of treatment in the individual case. C. C. LUND: Results of treatment of cancer of lip. GRANTLEY W. TAYLOR: Carcinoma of the mouth in the female. RICHARD DRESSER: Radiation treatment of oral carcinoma. CHARLES B. HOPKINS: Prophylaxis of cancer of the mouth. SOMERS STURGIS: Electrical currents between fillings of different metals as an etiological factor in leucoplakia and carcinoma of the mouth.

E. W. HERMAN and LEROY A. SCHALL—3:30. Carcinoma of the accessory sinuses, tonsils, and larynx.

MASSACHUSETTS WOMEN'S HOSPITAL

Thursday

HENRY T. HUTCHINS—9. Panhysterectomy.

STEPHEN RUSHMORE—9. Plastic laparotomy.

WILLIAM A. WHITE, JR.—9. Laparotomy.

REGINALD MARGESON—9. Transverse cervical cæsarean section.

ROBERT L. MASON—9. Thyroidectomy.

Staff—2. Dry clinic. CHARLES H. LAWRENCE: Endocrine sterility, end-results. DONALD MACOMBER: Problems of sterility. CHARLES F. PAINTER: Congenital obturator dislocation of right hip; causes of eburnation of bone. J. STEWART ROONEY: Pathological specimens.

FREE HOSPITAL FOR WOMEN

Tuesday

F. A. PEMBERTON, G. V. SMITH and S. C. GRAVES—9. Operative and dry clinic: Carcinoma of cervix uteri, treatment and results, prevention, diagnosis of early cases, relation to cervicitis and its treatment, complications of radium treatment, relief of pain; carcinoma of fundus uteri, treatment and results, classification; other tumors of uterus—fibroids, adenomyoma.

Wednesday

F. A. PEMBERTON, G. V. SMITH and PAUL YOUNGE—9. Operative and dry clinic: Tumors of the ovary, diagnosis, treatment, and results. Cystadenoma, granulosa cell tumor, Brenner tumor, teratoma; endometriosis, diagnosis and treatment; tumors of tubes, round ligaments, and vagina.

Thursday

G. V. SMITH and JOHN ROCK—9. Operative and dry clinic: Sterility, diagnosis, treatment and results; menorrhagia and metrorrhagia, diagnosis, treatment and results; endocrine research; dysmenorrhœa.

Friday

F. A. PEMBERTON, E. B. SHEEHAN and S. C. GRAVES—9. Operative and dry clinic: Prolapse, procidentia; complete tear of perineum; vesico- and rectovaginal fistulæ; kraurosis vulvæ, carcinoma vulvæ; Trichomonas vaginale; tumors of breast, value of X-ray treatment.

PONDVILLE STATE CANCER HOSPITAL

Tuesday—2

ERNEST M. DALAND. The Massachusetts cancer program.

HENRY JACKSON, JR. Some aspects of malignant lymphoma.

JOE V. MEIGS. Ovarian tumors.

LANGDON PARSONS. Treatment of cancer of the cervix by X-ray followed by radium.

ROGER GRAVES. Cancer of the prostate with metastases.

CHARLES KICKHAM. Cancer of the penis.

CHARLES DUMAS. X-ray treatment of advanced skin cancer.

Demonstration of cases.

Friday—2

GRANTLEY TAYLOR. Radium needles in cancer of breast.

HORATIO ROGERS. Chronic cystic mastitis.

RICHARD DRESSER. X-ray in the diagnosis of gastro-intestinal cancer.

SHIELDS WARREN. Changes in tumor tissue caused by radiation.

JOHN HODGSON. Treatment of pain in cancer patients.

CARL ERNLUND. Cancer of the antrum.

Demonstration of cases.

STATE PRISON COLONY

Thursday

HILBERT DAY. Practice of medicine in a modern correctional institution.

WILFRED BLOOMBERG. Psychiatric approach to prison medicine.

HENRY R. CRAIG. Unusual incidence of peptic ulcer in a prison population.

GEORGE H. LYONS. Minor surgical injuries in a protected population.

GEORGE ROTHBLATT. Dental conditions causing personality changes.

ROBERT B. BRIGHAM HOSPITAL

Monday

L. M. SPEAR—2. Classification of types of arthritis.
L. T. SWAIM and J. KUHNS—3. Treatment and orthopedic principles involved in arthritis.

Tuesday

H. K. THOMPSON—2. Clinical analysis of arthritis with reference to classification and treatment.
S. ROBERTS—3. Discussion of operative procedures, demonstration of end-results.

Wednesday

L. M. SPEAR—2. Classification of types of arthritis.
L. T. SWAIM and J. KUHNS—3. Treatment and orthopedic principles involved in arthritis.

Thursday

H. K. THOMPSON—2. Clinical analysis of arthritis with reference to classification and treatment.
S. ROBERTS—3. Discussion of operative procedures, demonstration of end-results.

MALDEN HOSPITAL

Wednesday

L. E. PHANEUF and N. A. GALLAGHER—9. Gynecological clinic, operative and dry. Complete tear of perineum, rectovaginal fistula; procidentia, subtotal hysterectomy; plastic and suspension operations. Treatment of abortions; treatment of benign uterine bleeding with radium.
R. SULLIVAN—9. Orthopedic clinic.
L. W. MCQUIRE—9. Amœbic dysentery and its complications.
C. F. LYNCH, D. J. DUGGAN, I. J. WALKER and F. W. GAY—2. Surgical operations.
Staff—2. Dry clinic. J. S. ROONEY: Pathological demonstration. I. J. WALKER: Discussion of jaundice with demonstration of liver specimens. L. SILVA: Discussion of coronary and gall-bladder disease in middle-aged people with electrocardiographic tracings. C. H. STAPLES: Hyperpituitarism, demonstration of cases.

NEW ENGLAND BAPTIST HOSPITAL

Tuesday

HALSEY B. LODER—9. Operative clinic.
Staff—9. Dry clinics. HALSEY B. LODER: Portal thrombosis; ulcerative colitis; gall stones, pancreatitis; uterine fibroids. A. A. HORNOR: Ulcerative colitis. SETH FITCHET: Surgery of congenital deformities of the extremities. JAMES L. POPPEN: Trigeminal neuralgia; spinal cord tumors. G. E. HAGGART: Skeletal traction in the treatment of fractures of the metacarpals, metatarsals and phalanges.

Thursday

F. H. LAHEY, H. M. CLUTE, R. B. CATTELL and R. H. OVERHOLT—9. General surgery, operative clinic.
GILBERT HORRAX and JAMES POPPEN—9. Neurosurgical operations.
G. E. HAGGART—9. Orthopedic surgery.
JAMES B. HICKS—9. Urological surgery.
LINCOLN F. SISE, PHILIP D. WOODBRIDGE and URBAN EVERSOLE—9. Anæsthesia.

HARVARD UNIVERSITY

Dillon Field House, Soldier's Field
Opposite Harvard Stadium, Allston, Mass.

Wednesday

AUGUSTUS THORNDIKE, JR.—2. Care and prevention of traumatic injuries in athletics; demonstration of protective strapping, padding, and apparatus used in modern athletics.

SURGERY OF THE EYE

MONDAY

F. H. VERHOEFF—Massachusetts Eye and Ear Infirmary—2. Operations.

J. J. REGAN, S. WEISS and DONALD MUNRO—Boston City Hospital—2. The eye in arteriosclerosis, hypertension and brain tumor.

V. G. CASTEN—Massachusetts Eye and Ear Infirmary—2. Visual fields in neurological cases.

T. L. TERRY—Massachusetts Eye and Ear Infirmary—2. Pathological demonstration.

J. H. WAITE and associate—New England Deaconess Hospital—2. The eye in diabetes.

W. B. LANCASTER—520 Commonwealth Ave.—2. The Eikonometer.

TUESDAY

H. B. C. RIEMER and assistant—Massachusetts Eye and Ear Infirmary—9. Operations.

A. J. BEDELL—Massachusetts Eye and Ear Infirmary—9. Technique in photographing the fundus.

HENRY M. EMMONS, WILLIAM D. ROWLAND and JOSEPH J. SKIRBALL—Massachusetts Memorial Hospitals—9. Operations.

J. S. FRIEDENWALD—Massachusetts Eye and Ear Infirmary—9. Slit-lamp ophthalmoscopy.

GILBERT HORRAX—New England Deaconess Hospital—9. Malignant exophthalmos.

PETER MCADAMS—St. Elizabeth's Hospital—11. Operations.

WEDNESDAY

J. H. WAITE and assistant—Massachusetts Eye and Ear Infirmary—9. Operations.

A. J. BEDELL—Massachusetts Eye and Ear Infirmary—9. Technique of photographing the fundus.

F. H. VERHOEFF and assistant—Massachusetts Eye and Ear Infirmary, Howe Laboratory—9. Demonstrations.

Staff—Carney Hospital—9. Operations.

JOSEPH J. SKIRBALL—Boston Dispensary—9. The eye and syphilis.

HUGH DONAHUE—St. Elizabeth's Hospital—11. Operation for cataract.

ALLEN GREENWOOD—Massachusetts Eye and Ear Infirmary—2. Fundus cases.

T. L. TERRY—Massachusetts Eye and Ear Infirmary—2. Contact glasses.

Staff—Massachusetts Eye and Ear Infirmary—2. Motion picture demonstration of operations.

J. J. REGAN, SOMA WEISS and DONALD MUNRO—Boston City Hospital—2. The eye in arteriosclerosis.

V. G. CASTEN—Long Island Hospital—2. Operative and dry clinic.

J. H. WAITE and associate—New England Deaconess Hospital—2. The eye in thyroid disease.

THURSDAY

E. K. ELLIS and F. H. VERHOEFF—Massachusetts Eye and Ear Infirmary—9. Operations.

H. B. C. RIEMER—Massachusetts Eye and Ear Infirmary—9. External diseases of the eye.

C. N. SPRATT and others—Massachusetts Eye and Ear Infirmary—9. Motion pictures of operations.

WILLIAM LIEBMAN and BENJAMIN SACHS—Beth Israel Hospital—10. Cataract extraction; muscle advancement; demonstration of cases.

HENRY M. EMMONS, WILLIAM D. ROWLAND and JOSEPH J. SKIRBALL—Massachusetts Memorial Hospitals—9. Dry clinic.

FRIDAY

W. H. LOWELL and ALLEN GREENWOOD—Massachusetts Eye and Ear Infirmary—9. Operations.

E. S. MCCARTHY—Massachusetts Eye and Ear Infirmary, Howe Laboratory—9. Color vision testing.

J. J. REGAN—Boston City Hospital—9. Operations.

V. G. CASTEN—Massachusetts Eye and Ear Infirmary—2. Neurological cases; ocular paralysis.

T. L. TERRY—Massachusetts Eye and Ear Infirmary—2. Pathological demonstration.

E. B. DUNPHY—Massachusetts Eye and Ear Infirmary—2. Traumatic cases, operations and results.

J. J. REGAN and W. B. CASTLE—Boston City Hospital—2. The eye in anæmic patients.

J. H. WAITE and associate—New England Deaconess Hospital—2. Cataract surgery in diabetes mellitus.

SURGERY OF THE EAR, NOSE, AND THROAT

MONDAY

H. DAVIS, H. A. DERBYSHIRE and M. H. LURIE—Harvard Medical School, Bldg.C—3. Physiological experiments on the hearing of animals with the technique first reported by Wever and Bray; report of the pathological conditions found in animals with abnormal hearing, demonstrating technique and apparatus used; physiological experiment conducted on animal with the apparatus used, demonstrating (1) auditory response obtained from the cochlea itself; (2) auditory response from the cochlear nerve and its various ganglion centers in the midbrain; (3) auditory response as obtained from the cortex in the temporal lobe; (4) effect of anæsthetics on these electrical responses; (5) demonstration of masking of tones in the cochlea.

TUESDAY

Staff—Massachusetts Eye and Ear Infirmary—9. Operations and demonstration of cases.

WALTER B. HOOVER—New England Deaconess Hospital—9. Osteoma of sinuses; laryngeal and tracheal complications of thyroid surgery; lingual tonsils and lateral bands of pharyngeal lymphoid tissue; syndrome of anæmia, glossitis, and dysphasia.

JOSEPH W. ROCKETT and THOMAS E. DINAN—Cambridge City Hospital—9. Tonsillectomies with gas-oxygen anæsthesia; cases of lateral sinus thrombosis.

F. G. MINITER and associates—Carney Hospital—9. Operation and demonstration of cases.

OLIVER A. LOTHROP—Newton Hospital—9. Tonsil, sinus and septum operations; reduction of recent fractures of the malar and nasal bones; discussion of the indications for mastoid and sinus surgery.

CHARLES I. JOHNSON, DONALD H. MACDONALD and EDGAR M. HOLMES—Newton Hospital—9. Operations and demonstration of cases.

ISABELLA D. KERR—New England Hospital for Women and Children—9:30. Avertin anæsthesia.

MARGARET NOYES KLEINERT—New England Hospital for Women and Children—9:30. Mastoidectomies in infants.

C. W. BUSH, R. O. PARRIS and B. N. WEIN—Massachusetts Memorial Hospitals—10. Operations.

F. E. GARLAND—Massachusetts Eye and Ear Infirmary, Hooper room—10. Demonstration of historical instruments.

WILLIAM T. HALEY—St. Elizabeth's Hospital—11. Operation for correction of dislocation of nasal septum.

H. L. BABCOCK—Massachusetts Memorial Hospitals—2. Otological problems in contagious diseases.

LEIGHTON F. JOHNSON—Massachusetts Memorial Hospitals—2. Otolaryngological clinic.

H. P. MOSHER—Harvard Medical School, Bldg. B—2. Exhibition of anatomical cases demonstrating the anatomy of the nose and throat; discussion of teaching methods; demonstration on the cadaver of the submaxillary approach for deep pus in the neck. P. E. MELTZER and M. H. LURIE: Exhibition of specimens illustrating the anatomy of the ear.

Staff—Beth Israel Hospital—2. L. M. FREEDMAN: Experiences with vocal cord paralysis in thyroidectomy. JACOB FINE: Technique for relief of bilateral recurrent nerve injury. CHARLES GETTES: Demonstration of technique for eliciting vestibular reactions by galvanism. L. M. FREEDMAN: Jugular puncture in mastoiditis. S. CLINE: Tuberculous laryngitis and its treatment. S. GARFIN: Treatment of malignant tumors of the upper respiratory tract. L. M. FREEDMAN: Bronchoscopic studies.

WEDNESDAY

Staff—Massachusetts Eye and Ear Infirmary—9. Operations and demonstration of cases.

WALTER B. HOOVER—New England Deaconess Hospital—9. Operations.

Staff—Children's Hospital—9. LYMAN RICHARDS: Acute laryngotracheobronchitis. MAURICE EVANS: Bilateral jugular ligation and its neurological complications. PHILIP MYSEL: Cerebral abscess. CHESTER MILLS: Sinusitis. JOSIAH E. QUINCY: Radical mastoid operation. CHARLES ALLMAN: Unusual foreign bodies. ELMER GILLESPIE: Complications in simple mastoidectomy. SAMUEL CLINE: Cases of sinus thrombosis.

HARRY J. INGLIS and associates—Boston Dispensary—9. Dry clinic. LOUIS WOLFSON: Bronchoscopy in the upright position as an out-patient procedure. A. I. COHEN, F. S. DUSHAN and FRANCIS STERN: An improved method of skin testing in allergic disturbances.

F. G. MINITER and associates—Carney Hospital—9. Operations and demonstration of cases.

LEIGHTON F. JOHNSON—Massachusetts Memorial Hospitals—10. Bronchoscopic operative clinic.

F. E. GARLAND—Massachusetts Eye and Ear Infirmary, Hooper room—10. Demonstration of historical instruments.

JOHN BURNS—St. Elizabeth's Hospital—11. Radical sinus operation under nerve block.

A. W. ROWE and D. W. DRURY—Massachusetts Memorial Hospitals—2. Endocrine factors in deafness.

THURSDAY

Staff—Massachusetts Eye and Ear Infirmary—9. Operations and demonstration of cases.

WALTER B. HOOVER—New England Baptist Hospital—9. Operations.

E. J. BUTLER and C. H. ALLMAN—Cambridge Hospital—9. Operative and dry clinic. Hæmatogenous infection of left mastoid with extradural abscess in a nine months old child; pneumococcus type III meningitis with labyrinthitis, demonstration of case.

F. G. MINITER and associates—Carney Hospital—9. Operations and demonstration of cases.

F. E. GARLAND—Massachusetts Eye and Ear Infirmary, Hooper room—10. Demonstration of historical instruments.

C. FAUNCE—Faulkner Hospital—11. Operations and demonstration of cases.

WILLIAM T. HALEY—St. Elizabeth's Hospital—11. Radical operation for maxillary antrum.

JOHN BURNS—St. Elizabeth's Hospital—11. Radical mastoid operation.

FRIDAY

Staff—Massachusetts Eye and Ear Infirmary—9. Operations and demonstration of cases.

WALTER B. HOOVER—New England Deaconess Hospital—9. Operations.

F. G. MINITER and associates—Carney Hospital—9. Operations and demonstration of cases.

Staff—Massachusetts Eye and Ear Infirmary—9. Dry clinic. H. P. CAHILL: The present status of brain abscess from the standpoint of the otologist. P. E. MELTZER: A twelve year summary of cases of lateral sinus thrombosis at the Infirmary. P. MYSEL: A ten year review of cases of labyrinthitis at the Infirmary. D. C. SMYTH: Chest cases requiring bronchoscopy, lantern slide demonstration. A. S. MACMILLAN and D. C. SMYTH: The accessory sinuses from the standpoint of the roentgenologist and the clinician. A. S. MACMILLAN: Petrositis from the X-ray standpoint. G. H. POIRIER: Result of the Mosher-Toti tear sac operation. M. H. LURIE: Histological slides showing the pathological condition of the internal ear. E. W. HERMAN: Radium and X-ray treatment of cancer of the larynx. HARRIS P. MOSHER: Notes on œsophageal cases. F. E. GARLAND: Surgery of the submaxillary gland. C. G. PAGE: Fungi in tracheal and bronchial mucous. GEORGE L. TOBEY, JR.: The Tobey-Ayer test.

F. E. GARLAND—Massachusetts Eye and Ear Infirmary, Hooper room—10. Demonstration of historical instruments.